American Journal of Diseases of Children

VOLUME 72 OCTOBER 1946 NUMBER 4

COPYRIGHT, 1946, BY THE AMERICAN MEDICAL ASSOCIATION

PRECLINICAL STAGE OF INFANTILE HYPERTROPHIC PYLORIC STENOSIS

ARVID WALLGREN, M.D.
STOCKHOLM, SWEDEN

AS IS well known, anatomic investigations have shown that the underlying cause of infantile pyloric stenosis is a muscular hypertrophy of the pyloric canal (or canalis egestorius) in conjunction with constriction of its lumen. This constriction of the lumen of the pyloric canal and the rigidity of the walls produced by the hypertrophy can be detected in living subjects by roentgenographic examination.[1] Runström,[2] perhaps the foremost authority on the roentgen appearances in the disease, describes the typical features in the following manner:

In the manifest stage of the disease, with the characteristic vomiting, the pyloric canal is obstructed so that its lumen for a distance of 2 to 3 cm. is only a few millimeters in width. The evacuation time of the stomach is delayed, and the contrast medium does not start to pass out into the duodenum until after one-half to two hours. The stomach is distended, and it displays stenosal peristaltic movements. The roentgen appearances are more or less the same after the cessation of the vomiting, but the lumen becomes slightly wider and numbers of longitudinal folds of mucous membrane are to be seen. The evacuation time, however, is now normal, and the contrast substance begins to pass out into the duodenum after five to fifteen minutes. This stage continues in all infants examined until the age of 1 to 4 years. As time goes on, small waves resembling the peristalsis begin to pass over the canal, and normal motility is soon reinstated.

These roentgenographically demonstrable changes are present in all manifest cases of the disease, and if the roentgen picture shows normality a diagnosis of infantile pyloric stenosis can in all probability be

From the Pediatric Department, Norrtulls Hospital, Royal Caroline Medical School.

1. Meuwissen, T., and Slooff, J.: Roentgen Examination of Pyloric Canal in Infants with Congenital Hypertrophic Pyloric Stenosis, Am. J. Dis. Child. **48**:1304 (Dec.) 1934.

2. Runström, G.: On the Roentgen-Anatomical Appearance of Congenital Pyloric Stenosis During and After the Manifest Stage of the Disease, Acta pædiat. **26**:383, 1939.

excluded. That these are the circumstances existing in this particular disease is agreed on by different authors.[3]

On the other hand, what has not hitherto been cleared up is the condition of the pyloric portion of the stomach before the appearance of clinical symptoms. The symptoms do not, as we know, arise immediately after birth but appear only after the passage of a few weeks, usually when the child is 3 weeks of age. This symptom-free interval between birth and the time when the clinical signs of stenosis in the form of vomiting make their appearance is a remarkable feature which is hardly compatible with the view that pyloric stenosis in infants is in general a congenital phenomenon.

It is conceivable that the muscular hypertrophy may be congenital but that the symptoms of obstruction do not become apparent until a more pressing demand for rapidity of movement is placed on the stomach as the child, a few weeks after birth, becomes strong enough to ingest a larger quantity of nourishment. Evidence supporting the theory that the muscular hypertrophy is congenital is the fact that children dying shortly after the appearance of the clinical symptoms already show appreciable hypertrophy, which could hardly have arisen simultaneously with the attacks of vomiting. As far as the clinical examination is concerned, there is no possibility of examining the children before the clinical symptoms of pyloric stenosis appear, for the purpose of establishing with certainty or excluding the presence of hypertrophy of the muscles of the pyloric canal. Palpation of the pyloric tumor is far too uncertain a method of examination to be of value in such cases; the chances of finding the tumor before clinical symptoms are manifested must be extremely small, and the growth is not always found even in the severe, manifest forms of the disease.

Now that there is available in roentgen examination a method for studying the condition of the pyloric canal in hypertrophic pyloric stenosis, it is possible to carry out in vivo investigations on this part of the stomach even in very young infants. If the examinations are made in accordance with all the rules, they are not in the least injurious to the child, and among the thousands of examinations carried out at the different roentgen departments in Sweden no mishaps have occurred nor have there been any signs of unfavorable effects on the children.

In an endeavor to ascertain the roentgen-anatomic appearances in infants with hypertrophic pyloric stenosis before the occurrence of the clinical symptoms, I planned in collaboration with G. Runström a systematic roentgenologic investigation of a large number of newborn

3. Andresen, K.: Roentgenologic Follow-Up Examination in Congenital Pyloric Stenosis After Manifest Stage, Acta pædiat. **27**:334, 1940. Voss, E. A.: Röntgenuntersuchung der hypertrophischen Pylorusstenose, Ztschr. f. Kinderh. **53**: 650, 1932.

infants. It was thought that among all those examined there might be 1 or possibly more in whom clinical symptoms of the disease would later develop.

It has been asserted in a previous paper [4] that manifest, that is to say roentgenologically observable, hypertrophic pyloric stenosis occurs in 1 of every 250 children in Sweden. In accordance with the consistently higher incidence among boys the frequency of pyloric stenosis among them is 1 in 150 and among girls 1 in 775. Girl babies, consequently, ought not to be used for an investigation such as the present one. As the object of the investigation was to control the condition in the roentgenologically examined infants after the newborn period, at the age when symptoms of pyloric stenosis might be expected to manifest themselves in any of the infants examined who would be subject to this disease, it was considered advisable also to exclude from the series all infants of whom a follow-up examination was liable to prove difficult or impossible. The obstetric clinic at Göteborg, where the examination of the newborn infants was to be undertaken, is a district institution which only in exceptional cases admits women from other parts of the country. These women's infants would not with absolute certainty be available for reexamination after their return home from the clinic. For this reason all infants whose mothers did not live in Göteborg were excluded. Although the actual roentgen examination has been found to be harmless and to cause no ill effects on newborn infants, it was naturally considered unwise to subject prematurely born infants or those who were weak, sick or suffering from birth injuries to this examination. These children also were excluded.

It was decided that, with the exception of the categories mentioned, a total of 1,000 newborn boys born consecutively at the Göteborg maternity clinic would be submitted to roentgen examination. After the examination all these infants were kept under supervision and controlled by infant welfare centers, and those displaying symptoms of vomiting were admitted to the medical department of the Children's Hospital for observation and a control roentgen examination. On the basis of the frequency figures previously mentioned, my associates and I calculated that among these 1,000 infants there should be 6 in whom pyloric stenosis would develop after the newborn stage. We succeeded in this way in securing 5 infants at the preclinical stage.

REPORT OF FIVE CASES

CASE 1.—This infant was born May 8, 1942. Roentgenograms were made on the fifth day of life. No changes were visible in the stomach or the duodenum.

4. Wallgren, A.: Incidence of Hypertrophic Pyloric Stenosis, Am. J. Dis. Child. **62**:751 (Oct.) 1941.

Peristaltic movements and evacuation were normal. There were no clinical symptoms. At 3 weeks of age the infant began to vomit. At the clinical examination gastric peristaltic waves were plainly visible. A second roentgen examination was performed when the boy was 3 months old. The pyloric canal was then seen to be constricted to a caliber of 2 mm. along a segment of about 3 cm. There were typical features of pyloric stenosis, with a normal evacuation time.

CASE 2.—This infant was born on May 29, 1942 and was given a roentgen examination on the fifth day of life. No changes were visible in the stomach or duodenum, and peristaltic waves and evacuation were normal. At this stage there were still no clinical symptoms. At the time of his arrival home from the hospital on the tenth day, projectile vomiting started. He was examined roentgenologically again at the age of 6 weeks. The stomach was seen to be distended, and it displayed typical stenosal peristaltic movements. Along a segment of 3 cm., the canal was constricted so that the lumen was not wider than about 3 mm. A time of forty minutes elapsed before the contrast medium passed out into the duodenum. There was typical pyloric stenosis, with a delayed evacuation time.

Fig. 1 (case 3).—*A*, a roentgenogram made on the seventh day of life. The canal is of normal width with peristaltic waves passing. *B*, a roentgenogram made one week after the manifestation of the clinical symptoms of infantile pyloric stenosis. The pyloric part of the stomach has now the shape of a canal 2 cm. long, with a lumen of a few millimeters. No peristaltic waves are passing over this part of the stomach.

CASE 3.—This boy was born March 20, 1942 and roentgen studies were made at the age of 7 days; no abnormality was observed in the stomach or duodenum (fig. 1 *A*). Peristalsis and evacuation were normal. At the age of 3 weeks he began vomiting with increasing intensity. A roentgen examination on April 23 (fig. 1 *B*), when he was 1 month old, showed a distended stomach and stenosal peristalsis. The lumen of the canal was no more than a few millimeters in width along a segment 2 cm. long, and longitudinal folds in the mucous membrane were distinguishable. At the end of about one hour a part of the stomach contents had passed through into the duodenum. The diagnosis was typical pyloric stenosis with a greatly delayed evacuation time.

CASE 4.—This boy was born May 13, 1942. A roentgenogram made when he was 5 days old showed complete normality. There were no clinical symptoms until May 26, when he began to vomit after his meal, the vomiting gradually becoming of the projectile type. Roentgenograms were made again on June 2,

when he was 20 days old. The stomach was greatly distended and displayed typical stenosal peristalsis. Fifteen minutes after the ingestion of the contrast meal the pyloric canal appeared on the roentgenogram as a narrow streak 2 cm. in length. There was a small amount of contrast medium in the bulb. After thirty-five minutes a small amount of the contrast medium had passed out into the small intestine. After one hour, more of the contrast medium had passed into the small intestine, but the greater part of it was still in the stomach. The diagnosis was typical pyloric stenosis, with a delayed evacuation time.

CASE 5.—The patient, born April 6, 1942, had a roentgen examination at the age of 4 days. The stomach was then normal as to shape and size (fig. 2 *A*). The peristaltic contractions were passing normally over the canal to the pylorus. The bulb was of normal shape and size. The time and rate of evacuation were normal. There were no clinical symptoms. Vomiting began shortly after the date of the examination, and the boy was therefore given another roentgen examination on April 30, when 24 days old (fig. 2 *B*). His stomach was seen to be distended, and there was typical pyloric peristalsis which ceased at a point about

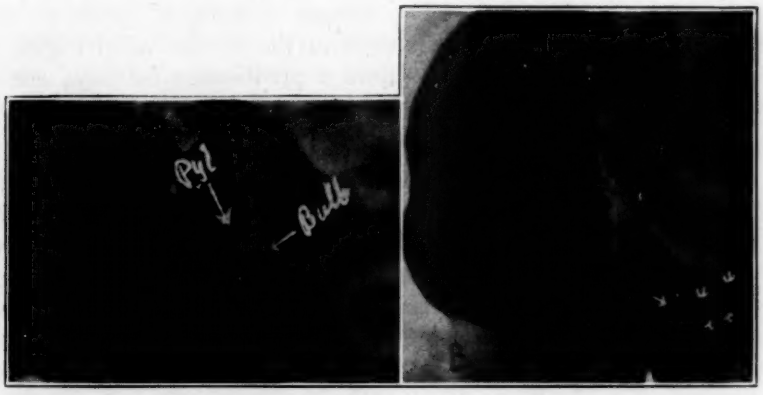

Fig. 2 (case 5).—*A*, roentgenogram on the the fourth day of life. Conditions are normal. There is no narrowing of the pyloric canal. *B*, roentgen examination at the age of 24 days, some time after the manifestation of the clinical symptoms of infantile pyloric stenosis. There are now no peristaltic waves passing the pyloric part of the stomach, which is changed into a narrow canal, 2 cm. in length.

2 cm. from the pylorus. Below this point the canal was constricted, the lumen being about 2 mm. wide, with longitudinal folds of mucous membrane. At the end of thirty minutes only a small amount of the contrast medium had passed into the duodenum. There was typical pyloric stenosis, with a slightly delayed evacuation time.

COMMENT

For the 5 children in whom pyloric stenosis later developed there was the same roentgen picture during the newborn period as for the 995 children who remained free from symptoms of the disease. Thus, in none of the 5 cases was a preformed stenosis of the pyloric canal to be seen on the roentgenograms. It is therefore hardly correct to speak of congenital pyloric stenosis. A remarkable feature is the

swiftness with which the roentgenographic pathognomonic signs appear. Within a couple of weeks the pyloric canal becomes constricted to such a degree that the lumen appears merely as a narrow streak, and its muscle becomes rigid and immobile. A roentgen examination cannot, of course, exclude the possibility that a certain increase in the muscular walls of the pyloric canal may be present during the preclinical newborn period. If preformed hypertrophy of the musculature does exist, it must be of such a nature as not to prevent the muscle from functioning and from producing the same roentgen picture as in a child not having this abnormality. It must be soft, must permit the passage of the peristaltic waves coming from the body of the stomach, must have no constricting effect and must not be in a state of permanent contraction or spasm.

The result of this investigation can hardly be said to have thrown any fresh light on the problem of the pathogenesis of hypertrophic pyloric stenosis in infants. The disease appears, if anything, still more puzzling. Just why the muscle in the pyloric canal begins to thicken and why this anomaly shows a predilection for boys are as much of an enigma as ever.

SUMMARY

The stomachs of 1,000 newborn boys were examined roentgenologically and found normal in every case; there was no sign of muscular hypertrophy of the pyloric canal nor of any retention, and the peristaltic waves passed over the canal in a normal way. All infants were supervised and controlled by the infant welfare centers. At 3 weeks of age 5 of them began to vomit, and a new examination a little later revealed clinical and roentgenologic signs of manifest hypertrophic pyloric stenosis. In these children the muscular hypertrophy which is the basic anatomic cause of the disease was not congenital but developed in an astoundingly rapid manner with typical symptoms shortly before the disease manifested itself.

CONGENITAL DEAFNESS AND OTHER DEFECTS FOLLOWING GERMAN MEASLES IN THE MOTHER

LOUISE A. HOPKINS, M.S.
NORTHAMPTON, MASS.

NEW light has recently been thrown on the etiologic factors involved in certain congenital malformations by three series of cases reported from Australia, in which virus infections, particularly German measles occurring early in pregnancy, seemed to be definitely related to the congenital defects.

In 1941, Gregg [1] reported a series of 78 cases of congenital cataract in infants whose mothers had had German measles early in pregnancy. Congenital heart disease was also present in 44 of these infants. Later Swan [2] and his co-workers confirmed the findings of the earlier study and reported a series of 49 cases of rubella during all stages of pregnancy, in 25 of which the rubella occurred in the first two months. Of a total of 31 children with congenital malformations, there were 17 with congenital cardiac lesions, 14 with congenital eye defects, 1 with mongolism, several with microcephaly, hypospadias and mental retardation and 7 deaf-mutes. Many of the infants had several defects. In a later paper Swan [3] reported 10 more cases of congenital malformations in infants whose mothers had had rubella in the early months of pregnancy. Reese [4] was the first American to report on this subject, and he noted 3 cases of congenital cataract and congenital heart disease in infants whose mothers had had rubella early in pregnancy. In 1944

From the Research Department of the Clarke School for the Deaf.

1. Gregg, N. M.: Congenital Cataract Following German Measles in Mother, Tr. Ophth. Soc. Australia **3**:35, 1941.

2. Swan, C.; Tostevin, A. L.; Moore, B.; Mayo, H., and Black, G. H. B.: Congenital Defects in Infants Following Infectious Diseases During Pregnancy, with Special Reference to Relationship Between German Measles and Cataract, Deaf-Mutism, Heart Disease and Microcephaly, and to Period of Pregnancy in Which Occurrence of Rubella Is Followed by Congenital Abnormalities, M. J. Australia **2**:201-210 (Sept. 11) 1943.

3. Swan, C.; Tostevin, A. L.; Mayo, H., and Black, G. H. B.: Further Observations on Congenital Defects in Infants Following Infectious Diseases During Pregnancy, with Special Reference to Rubella, M. J. Australia **1**:409-413 (May 6) 1944.

4. Reese, A. B.: Congenital Cataract and Other Anomalies Following German Measles in the Mother, Am. J. Ophth. **27**:483-487 (May) 1944.

Erickson [5] reported 11 more cases, of which he wrote: "Most of the babies were small and had considerable feeding difficulties. None of the babies were cyanotic and their cardiac physical findings made it seem likely that the defect was a patent interventricular septum. In no case was there a family history of congenital eye or cardiac anomalies." All 11 had congenital ocular defects, 9 had congenital cardiac defects, 2 were mentally retarded and 1 had severe anemia resembling erythroblastosis fetalis. Rones [6] reported 4 more cases of infants with ocular defects. In the 2 cases in which rubella occurred in the second month of pregnancy, the infants had cataracts, while in the 2 cases in which it occurred in the third month, they had congenital glaucoma.

These and other reports which have appeared in the literature have stimulated me to go over the data which have been collected at the Clarke School for the Deaf to see if there were any mothers of these pupils who had had German measles during the early months of pregnancy. Letters were written to the mothers of all the children, with omission only of those cases in which there was a definite history of infection in the child (those in which the child had had cerebrospinal meningitis and a few cases in which there was a definite history of speech before the onset of mumps with a history of profound deafness following the mumps) and those cases in which there was a definite history of deafness in the family. In other words, I wrote to the mothers when there was any doubt as to the cause of the deafness and to all mothers with only 1 child if his deafness was the only instance of deafness in the family so far as I had been able to determine. Many of these cases had already been classified in the records as hereditary or probably hereditary, but there was still some doubt in my mind as to the cause of of the deafness.

Table 1 shows the results of my inquiries:

TABLE 1.—*Incidence of German Measles During Pregnancies of Mothers of Deaf Children*

Number of Mothers Receiving Letters	Number of Replies	Number with German Measles During Pregnancy	Number with Other Virus Disease During Pregnancy
129	116	10	2

Table 2 shows in detail the data concerning the 10 children whose mothers had German measles during pregnancy.

5. Erickson, C. A.: Rubella Early in Pregnancy Causing Congenital Malformations of Eyes and Heart, J. Pediat. **25**:281-283 (Oct.) 1944.

6. Rones, B.: The Relationship of German Measles During Pregnancy to Congenital Ocular Defects, M. Ann. District of Columbia **13**:285-287 (Aug.) 1944.

TABLE 2.—*Data Concerning Children Whose Mothers Had Rubella During Pregnancy*

Ped. Number	Sex	Birth Date	Duration of Pregnancy at Onset Rubella, Mo.	Congenital Hearing Defects	Congenital Eye Defects	Congenital Cardiac Defects	Other Defects
102	M	1/ 7/27	1	Profoundly deaf	Congenital blindness in left eye; right eye normal	Congenital malformation; probable patent interventricular septum	Rickets; probable mental retardation
342	F	1/ 2/36	1	Partially deaf	None	None	Mentally retarded
326	F	1/13/36	At beginning of 2d	Partially deaf	Convergence and congenital cataract	Patent ductus arteriosus or anomaly of the aortic valve cusps, possibly bicuspid with regurgitation	At 4 years weight 24 pounds (11 Kg.), height 36 in. (91 cm.); died of measles June 1941 after 3 days' illness
329	M	1/ 4/36	At beginning of pregnancy	Partially deaf	None	Systolic murmur transmitted throughout cardiac area, at 10 years	Hyperactive; at 6 years weight 30 pounds (13.6 Kg.), height 37.5 in. (95 cm.); at 10 years weight 44 pounds (20 Kg.), height 49 in. (124 cm.)
329	F	12/23/35	2	Profoundly deaf	Left internal strabismus	Patent interventricular septum; tachycardia and slight right ventricular preponderance	Mentally retarded; at 5 years weight 28 pounds (12.7 Kg.), height 37 in. (94 cm.); at 10 years weight 48 pounds (22 Kg.), height 49 in. (124 cm.)
347	F	10/ 4/35	2 or 3	Profoundly deaf	None	None	None
266	F	11/18/28 (Fraternal twin to next child)	4	Partially deaf; right ear better	None	None	Possible mental retardation; thyroidectomy 1943
268	F	11/18/28	4	Profoundly deaf; left ear better	None	None	Possible mental retardation
368	F	9/ 9/36	4	Partially deaf; left ear better	Right internal strabismus	None	Possible mental retardation
324	M	12/ 4/35	6	Profoundly deaf	None	None	Poor muscular coordination and awkward gait
240	M	1/13/31	6	Profoundly deaf	None	None	None

There is still some doubt as to the cause of the deafness in 2 of the children in table 2. As to pedigree 329, though the mother of the child did have German measles during the second month of pregnancy and the child's defects seem to fit the general picture, the mother had a deaf brother whose deafness was reported to have been caused by "many gatherings in his head as a baby and small child." However, his deafness may have been congenital, and the deafness of the child with pedigree 329 might have been inherited and not the result

TABLE 3.—*Mothers with a Virus Disease Other Than Rubella During Pregnancy*

Ped. No.	Sex	Birth Date	Duration of Pregnancy at Onset of Influenza, Mo.	Congenital Hearing Defects	Congenital Ocular Defect	Congenital Cardiac Defect	Other Congenital Defects
322	F	11/20/26	1	Profoundly deaf	None	None	Mentally retarded
113	F	6/15/19	2	Profoundly deaf	None	None	Fragilitas ossium but no blue sclera

TABLE 4.—*Data Concerning Defective Children Whose Mothers Had no Virus Disease*

Ped. No.	Sex	Birth Date	Congenital Hearing Defects	Congenital Ocular Defects	Congenital Cardiac Defects	Other Congenital Defects
125	F	2/ 6/29	Profoundly deaf	None	None	Pyloric stenosis; though born at term, the child weighed only 4 pounds (1,814 Gm.), had no finger nails, no toe nails, eyebrows or eyelashes at birth. The twin brother weighed 6½ pound (2,948 Gm.) and was normal in every way
239	M	4/ 9/31	Profoundly deaf	None	None	Pyloric stenosis; hyperactive
362	M	5/ 6/38	Partially deaf	None	None	Congenital lack of right ear
366	M	9/24/35	Partially deaf	Weak eye muscle	Congenital heart murmur	Mentally retarded; at 7 years weight 35 pounds (16 Kg.), height 42 in. (107 cm.); at 10 years weight 45 pounds (20 Kg.), height 48.5 in. (123 cm.)
364	M	6/21/35	Profoundly deaf	Left internal strabismus	None	None
128	F	10/16/28	Profoundly	None	Congenital heart defect	Hyperactive; at 4 years weight 28 pounds (12.7 Kg.), height 36 in. (91 cm.); suggestion of ankle clonus

of the German measles which her mother had during early pregnancy. In pedigree 324, the boy would also have to be placed in a group with unknown causes of deafness. Although his mother had German measles during the sixth month of pregnancy, this period is regarded by many doctors as too late in the developmental history of the fetus to permit any profound disturbance by the virus of rubella, especially with respect to disturbances in the eye, ear or heart.

In pedigrees 240, 266 and 368 the onset of the German measles in the mother was in the fourth month or later, but we have been unable to find any other possible cause for the deafness.

In table 3 data are shown concerning the 2 cases in which the mother did not have German measles during pregnancy, but did have another virus disease, namely influenza,

Table 4 shows in detail the data concerning 6 cases in which the mother had no virus disease of any kind during pregnancy, yet the children present defects which are supposed to be caused by the mothers having German measles during pregnancy.

COMMENT

It should be noted that in analyzing the replies from the 10 mothers who had had German measles during pregnancy I found that 7 of these were mothers of present pupils and the other 3 were mothers of pupils who had left school some time ago. Of 67 mothers of former pupils who replied 3, or 4.4 per cent, stated that they had had German measles, and of the 49 mothers of present pupils who replied 7, or 14.5 per cent, had had German measles.

The fact that the second percentage is over three times the first might be interpreted as due to the fact that the mothers of present pupils remember details of their pregnancies better than those of former pupils who were born much longer ago or that German measles is becoming more virulent and is now causing defects whereas formerly it did not. Whichever fact is true, German measles must actually have occurred in many more mothers in the earlier group, but was regarded as of so little importance that it was not remembered.

CONCLUSIONS

It is suggested that rubella occurring early in pregnancy may be the cause of certain cases of congenital deafness that have formerly been unexplained. Ten such cases are reported in which the mother had German measles during pregnancy. The various defects found in the offspring are listed.

Two cases in which the mother did not have German measles but did have another virus disease, namely influenza, and 6 cases in which the mother did not have any virus disease during pregnancy but in which the child exhibited some of the same congenital defects are also listed. All children here reported are or have been pupils at the Clarke School for the Deaf.

REENFORCING OR "BOOSTER" INJECTION OF PERTUSSIS VACCINE IN PREVIOUSLY IMMUNIZED CHILDREN OF KINDERGARTEN AGE

Pertussis Field Series V

PEARL KENDRICK, Sc.D.

GRACE ELDERING, Sc.D.
AND
MARY THOMPSON
GRAND RAPIDS, MICH.

THE PRESENT study is the fifth of the several pertussis immunization series in Grand Rapids during the past dozen years. In series I, reported in 1939,[1] protection was demonstrated following pertussis vaccination; in series II and III, reported in 1943,[2] protection was shown to follow immunization with an alum-precipitated vaccine and also with an alum-precipitated combined diphtheria toxoid and pertussis vaccine. In series IV, further observations are being made on the alum-precipitated combined antigen, and in series VI a combination fluid diphtheria toxoid and pertussis vaccine is being studied.

In series V the main objective was to study the effect of a reenforcing, or "booster," injection of pertussis vaccine on kindergartners who had received their original course of immunization at the city immunization clinics and for whom therefore we had definite records. Another objective was the tabulation of histories on all the children entering kindergarten, with respect to whooping cough and to pertussis vaccination, and correlation of these histories with subsequent records of reported cases of whooping cough.

METHODS

Whole Study Group.—All children who entered kindergarten in Grand Rapids in the terms beginning September 1942 and February 1943 were entered in the series. School nurses and teachers obtained histories from the parents regarding the whooping cough record of each child prior to entry and also his record of pertussis vaccination. These records were checked against the laboratory files of children given injections of pertussis vaccines at the clinic in previous series.

From Michigan Department of Health, Bureau of Laboratories, Western Michigan Division.

1. Kendrick, P.; Eldering, G., and Borowski, A.: A Study in Active Immunization Against Pertussis, Am. J. Hyg. **29**:133-153 (May) 1939.

2. Kendrick, P. L.: A Field Study of Alum-Precipitated Combined Pertussis Vaccine and Diphtheria Toxoid for Active Immunization, Am. J. Hyg. **38**:193-202 (Sept.) 1943.

Group for "Booster" Injection.—Lists of children previously immunized at the city clinics were prepared by the district and by the school. Health department nurses in the different districts called on the parents and offered a "booster" injection at a clinic. Since this was the first use of the "booster" injection, it was necessary to explain the procedure to the families. The nurse was instructed to make the following points: The child had a course of pertussis vaccine more than a year ago; all immunization has a tendency to become weaker after considerable time has passed; when the child starts school the chances for exposure to whooping cough are unusually great; a "booster" injection is offered for the purpose of strengthening the immunity; opsonic tests will be made before and after the "booster" injection to find out what effect the injection has had.

Vaccine for "Booster" Injection.—Plain pertussis vaccine, 10,000,000,000 organisms per cubic centimeter, prepared in the Michigan Department of Health laboratories, was given in a dose of 0.5 cc.

Records and Follow-up.—A permanent card was made for each child, with his history prior to entry, and subsequent observations were recorded. The cards were checked against lists of reported cases furnished monthly by the city health department. Each child reported to have whooping cough was visited by the nurse assigned to the study, and a case history was obtained as in the previous series. Observations were continued through June 30, 1944.

Procedure for Opsonocytophagic Tests.—The methods for testing the opsonocytophagic reaction have been described elsewhere.[3] Briefly, 0.1 cc. of whole blood obtained from the finger is mixed with a solution of sodium citrate. One tenth cubic centimeter of a suspension containing 20,000,000,000 Hemophilus pertussis organisms per cubic centimeter killed with merthiolate is mixed with the blood, and this mixture is incubated at 37 C. for thirty minutes. Preparations on slides are then made as for differential blood counts and stained with filtered Hastings stain. Twenty-five polymorphonuclear cells are observed, and the cells are recorded as to the number of bacilli phagocytosed in the ranges 0, 1 to 5, 6 to 20, 21 to 40 and 41 or more, in order to arrive at a figure to represent the relative strength of the reaction. These ranges have been assigned the arbitrary factors 0, 1, 3, 8 and 12 respectively. The products of the number of cells in each range and the respective factors are determined, and these products are added to give the figure used to measure the relative strength of opsonic reaction for purposes of comparison.

An example of how the results are expressed is given in the following tabulation.

Number of bacilli phagocytosed.....	0	1 to 5	6 to 20	21 to 40	41 or more
Assigned factor	0	1	3	8	12
Example based on counting 25 cells: number in each range.....	2	5	8	5	5
Product: number of cells × factor.....	0	5	24	40	60
Sum of products.....			129		

Based on the results of many tests before and after immunization, the strength of reaction in relation to the sum of the products is considered roughly as follows: 0 to 25, negative; 26 to 100, weak; 101 to 200, moderate, and 201 and more, strong.

3. Kendrick, P.; Gibbs, J., and Sprick, M.: The Opsonocytophagic Test in the Study of Pertussis, J. Infect. Dis. **60**:302-311 (May-June) 1937. Kendrick, P.; Lawson, G. M., and Miller, J. J.: Hemophilus Pertussis: Diagnostic Procedures and Reagent, ed. 2, New York, American Public Health Association, 1945, pp. 172-175.

OUTLINE OF MATERIAL FOR STUDY

The basic data for study are tabulated below, including a classification according to records of whooping cough and of pertussis vaccination prior to entry to the kindergarten.

1. Number of children in series V 2,735
   (Kindergartners entered in Grand Rapids schools September 1942 and February 1943, excepting 46 for whom no histories were obtained)
2. History with reference to pertussis vaccine
   - A. Number with record of pertussis vaccination 1,455
     - (a) Vaccine in health department clinics 857
     - (b) Vaccine by private physicians 598
   - B. Number with record of no pertussis vaccine 1,280
3. History with reference to whooping cough
   - A. Number with record of attack of whooping cough 437
     - (a) No pertussis vaccine 357
     - (b) Vaccine by family physician 46
     - (c) Vaccine in health department clinics 34
   - B. Number recorded as not having had whooping cough 2,298
     - (a) No pertussis vaccine 923
     - (b) Vaccine by family physician 552
     - (c) Vaccine in health department clinics 823
4. A "booster" injection of 0.5 cc. of plain pertussis vaccine was offered to the 823 children who had received their primary course of injections in the health department clinic and who presumably had not had whooping cough
   Number who received "booster" injection 408
5. Opsonocytophagic tests
   - A. Number tested before "booster" injection 275
   - B. Number of these tested both before and after the "booster" injection 187

RESULTS OF STUDY

Histories Prior to Entry into Kindergarten.—From the outline of basic material for study, it is seen that of the 2,735 kindergartners for whom histories were available, 1,455, or 53.2 per cent, had received vaccine. Of these, 857, or 59 per cent, had received vaccine in city

TABLE 1.—*Number of Children with History of Vaccination Against Pertussis and with Record of an Attack of Whooping Cough Prior to Entry in Kindergarten*

Whooping Cough Prior to Entry in School	Pertussis Vaccine Record of Children Prior to Entry in School				
	Number of Children Vaccinated			Number of Children Not Vaccinated	Total
	In Clinic	Outside of Clinic	Total		
No	823	552	1,375	923	2,298
Yes	34	46	80	357	437
Total	857	598	1,455	1,280	2,735
Per cent of each group who had whooping cough	4%	8%	6%	28%	16%

health department clinics in connection with one or another of the pertussis field series; 598, or 41 per cent, had been vaccinated by private physicians, and no records were available as to the kind of vaccine used. In table 1, the records of whooping cough prior to entry in school are correlated with pertussis vaccination prior to entry.

While such data derived from information given by mothers to the school nurse are rough and subject to error, the relatively larger percentage of recorded attacks among the children who received no vaccine in comparison with the vaccinated children is consistent with the results of the previously reported field studies.

Opsonocytophagic Tests Before "Booster" Injection.—The effect of the "booster" dose of 0.5 cc. of plain pertussis vaccine was studied with particular reference to the child's opsonocytophagic response. Observations on this phase of the study were discussed at a meeting of the Society of American Bacteriologists in 1944 [4] and are amplified here.

Correlation with the Kind of Antigen Used for Primary Immunization.—Combined diphtheria toxoid and pertussis vaccine had been used for primary immunization of 28 of the 275 children tested before they received a "booster" injection: plain pertussis vaccine for 144; and

TABLE 2.—*Opsonocytophagic Reactions in 275 Children After Primary Pertussis Immunization According to the Interval Which Had Elapsed*

Interval Between Primary Immunization and Test, Years	Number Tested	Opsonocytophagic Tests, Average Reaction
1 or less than 1	31	136
2	21	148
3	58	142
4	143	144
5	22	117
All intervals	275	142

alum-precipitated pertussis vaccine for 103. The vaccine had been given in three 1 cc. injections four weeks apart. No significant difference was found.

Correlation with Interval Between Primary Immunization and "Booster" Injection.—In table 2 the results for all 275 children tested before the "booster" injection are correlated according to the interval which had elapsed since primary immunization.

Previous experience suggests that the strongest reactions are to be expected around two months after immunization, and the results, therefore, in the first interval charted may be considered to have dropped considerably below the peak reaction. The results suggest little change in the opsonic levels from 6 months to 4 years. The result in the fifth year is lower, but is based on only 22 children.

Opsonocytophagic Tests After "Booster" Injection.—Opsonocytophagic tests after the "booster" injection were made on 187 of the

4. Kendrick, P. L.; Eldering, G., and Thompson, M.: Effect of a Booster Dose of Pertussis Vaccine on Opsonic Response in Children, abstracted, J. Bact. **49**: 202 (Feb.) 1945.

275 who were tested before. Here again, no significant difference was observed in relation to the kind of antigen used for primary immunization. The results in relation to the interval between primary and "booster" injections are given in table 3.

TABLE 3.—*Opsonocytophagic Reactions in 187 Children Before and After a "Booster" Injection of Plain Pertussis Vaccine According to the Interval Between Primary and "Booster" Immunization*

Interval Between Primary Immunization and "Booster" Dose, Years	Number Tested	Opsonocytophagic Tests Before and After the "Booster" Dose: Average Reaction		Ratio of Results after "Booster" Dose to Results Before
		Before	After	
6 to 12 months	23	150	229	1.5
2	12	147	226	1.5
3	37	144	237	1.7
4	102	145	231	1.6
5	13	112	196	1.8
All intervals	187	144	230	1.6

In judging the data on the basis of the average strength of reaction, as is done in tables 2 and 3, it should be noted that variability of reaction is great. In table 4, this is partly overcome by classifying the data under several ranges of reaction.

The general shift from the lower ranges of reaction to the higher following the "booster" vaccination is obvious. While only 23 per

TABLE 4.—*Opsonocytophagic Reactions in Children Tested Both Before and After a "Booster" Injection of Plain Pertussis Vaccine*

Summary of Results at All Intervals

Before and After "Booster" Dose		Range of Reaction: Weak to Moderate 26 to 50	51 to 100	101 to 150	151 to 200	Strong 201 to 250	251 to 300	301 and Over	Totals
Number	Before	5	50	50	39	31	12	0	187
	After	0	1	12	26	74	73	1	
Per cent	Before	3%	27%	27%	20%	17%	6%	0%	100%
	After	0	0.5%	6%	13%	40%	40%	0.5%	
	Before		77%				23%		100%
	After		20%				80%		

cent of the children had ratings in the strong range of reaction, over 200, before, 80 per cent of them had strong reactions after, the "booster" injection.

Reported Cases of Whooping Cough in the Series.—From the time of entry into kindergarten during the terms beginning September 1942 and February 1943 through June 30, 1944, when the study was closed, 79 cases of whooping cough were reported in the series. In addition to the 79 cases reported in the study group, 1 case was reported of a

child with a record of an attack previous to entry in school. The distribution of the cases according to the histories is outlined in table 5.

The incidence of pertussis in the entire study group according to cases reported to the city health department was extremely low. Of the 8 patients among the 823 children receiving injections at the clinic, 3 had had a "booster" injection and 5 had not. Twelve cases were reported for the children who received vaccine elsewhere than at the

TABLE 5.—*Reported Cases of Pertussis Subsequent to School Entry*

Vaccination Record	Number in Group	Reported Cases	
		Number	Per Cent
Vaccination by private physicians prior to school entry	552	12	2.1
Vaccination at clinic prior to school entry	823	8	0.9
"Booster" injection	(408)	(3)	0.7
No "booster" injection	(415)	(5)	1.2
No vaccine prior to school entry *	923	59	6.4
Totals	2,298	79	

* All names in the study list were checked with the records of vaccination received from the city health department. The only records we have of vaccine injections during the observation period (from the entry to close of the study) in children who had a history of having received no vaccine at the time of entry, are: 2, full course at clinic; 6, incomplete course at clinic; 3, injections by private physicians. None of these children were reported as having had whooping cough during the observation period.

clinic, an incidence of 2.1 per cent. Among the 923 children without vaccine, 59 were reported to have contracted the disease, an incidence of 6.4 per cent.

While the numbers of patients reported to have pertussis are too small to permit analysis with respect to the "booster" injection, their distribution among vaccinated and unvaccinated children is in accordance with the results reported for previous series.

COMMENTS

It seems worthy of note that the level of opsonic response remained moderately high even after four years. There is an apparent drop at five years, but relatively few children were tested at that interval. The question might be raised of the possibility that some of these children had a secondary stimulus due to exposure or to an unrecognized attack.

Another point that stands out is the similarity in the relative rise in the level of opsonic response following a "booster" injection regardless of the interval which has elapsed since the primary course of injections of vaccine. A point which is not so apparent in the summarized averaged results is the great range in reactions at all intervals. Since this was true also for the different antigen groups, the answer probably lies in individual variation in response.

The question that always arises with a study such as this concerns the correlation between the amount of circulating antibody and the

degree of protection. It is almost impossible to collect enough data of the kind required to give a significant answer. It seems reasonable, however, to assume that in general the child whose serum shows a strong in vitro response to the pertussis antigen is more likely to have protective antibody. Further, it would seem desirable to give a "booster" injection to assure a high antibody level, particularly at the time when the child is approaching the age band of the highest incidence of pertussis.

SUMMARY

Immune response as measured by the opsonocytophagic reaction was studied in a group of 187 children before and after a stimulating injection of plain pertussis vaccine given at the time of entry into kindergarten.

Tests before the "booster" dose suggested that a moderately high level of opsonic activity was maintained for as long as four years after primary immunization, with the three antigens used.

Tests after the "booster" injection showed reactions on the average 1.6 times those before the injection, and the average increased from the moderate range to that of strong reaction.

The results lend experimental support to the policy of giving a "booster" injection of pertussis vaccine to children just before they start to school when the likelihood of exposure to whooping cough is greatly increased.

Members of the City Department of Health of Grand Rapids cooperated in all phases of the work. In particular, Dr. C. C. Slemons, health officer, aided in the evaluation of the diagnoses, and supervising nurses Zenna Bruggink and Gertrude Levandoski gave further assistance.

The Board of Education of the city cooperated in the study, particularly the kindergarten teachers, who aided in accumulating the histories.

Follow-up work was done by Margaret Damon. Dorothy Maring assisted in tabulating the results.

Financial assistance was given by the Bureau of Maternal and Child Health of the Michigan Department of Health, with a grant from the funds of the Children's Bureau.

SPEECH THERAPY FOR CHILDREN WITH CEREBRAL PALSY

M. A. PERLSTEIN, M.D.
CHICAGO
AND
MARIE SHERE, M.S.
URBANA, ILL.

IT HAS been estimated that about 75 per cent of all children with cerebral palsy have speech defects and that from 50 to 75 per cent of these children can be benefited by speech training.[1] The value of such training cannot be overestimated. It is a vital part of the rehabilitation program because speech gives the child a chance to express himself, and, consequently, to acquire a more pleasing personality; it stimulates mental growth, and it improves his chance of becoming self supporting. In the case of some persons who, as a result of severe generalized involvement, are bedridden or confined to a wheel chair, speech is of prime and greatest importance—greater than self help or locomotion.

The purpose of this paper is to comment on some of the various types of speech defects which are found and to suggest certain therapeutic measures to be used in dealing with them.

All comment on speech training presupposes that the child is mentally able to profit thereby. However, it should be understood by all those who, in any capacity, work with children suffering from cerebral palsy that care must be taken not to diagnose a child's condition as feeblemindedness simply because he fails in any or all of the standard tests which are used to measure intelligence. All mental testing must be tentative; no one test or battery of tests yet devised will give a true picture of the educability of the child with cerebral palsy. Indeed, his very lack of speech constitutes an obstacle to accurate testing. Thus, it is obviously unfair to indict him on the basis of existing intelligence tests.

One would not call a crippled child feebleminded because he did not obey a command to walk. Yet if a child fails to speak intelligibly, or indeed to speak at all; if he drools; if he makes clumsy, awkward movements with a thick tongue, or frowns, squints and grim-

---

The authors are medical consultant and speech therapeutist respectively at the Cerebral Palsy unit of St. John's Crippled Children's School and Hospital, Springfield, Ill.

1. Pusitz, M. E.: Speech Correction in Cerebral Palsies, J. Speech Disorders **4**:209-218, 1939.

aces, there are many—and this includes physicians—who are ready to write him off as uneducable. Defective speech, visual and auditory loss and motor handicaps should all be taken into consideration, and the child should be given the benefit of any doubts as to his educability. It has been estimated that only one third of the children with cerebral palsy are actually feebleminded, one third have slight to moderate retardation, while one third have from average to superior intelligence.[2]

Before any therapy is undertaken, a complete diagnostic physical examination should be given the child to determine the nature of the motor difficulty. In addition to the neurologic, orthopedic and pediatric evaluation, visual, auditory and speech tests should be made. In the speech tests, toys, objects and pictures the names of which involve the use of various sounds in initial, medial and final positions are used to ascertain which sounds are defective or not present. About 45 per cent of the children with cerebral palsy have involvement of the athetoid type; about 40 per cent have the spastic type, and the remaining 15 per cent belong to groups having rigidity, ataxia and rarer types of manifestations.[3] In this discussion, we shall consider only the first two groups.

It is not always easy to distinguish between athetosis and spasticity. It is simple enough to say that the etiologic difference lies in the position of the cerebral lesion. If it is in the cortex or subcortical region of the motor and premotor areas or if it involves the pyramidal tract, spasticity is the result; if it is in the basal nuclei on one or both sides, there is athetosis. Also it seems simple to say that the former is characterized by prolonged, involuntary tonic spasms due to stretch reflexes induced by attempted motion and the latter by involuntary shifts of tonus from one group of muscles to another with constant, purposeless movements as the result. However, the actual diagnosis is not always that simple. The athetoid patient, because of his habitual, voluntary effort to control his movements, may appear spastic; the spastic patient, on the other hand, because of overflow motions, may produce what appears to be athetosis. However, the fundamental steps in teaching speech to spastic and to athetoid children do not differ greatly. In either case, relaxation is essential before any other form of treatment is instituted. It should be pointed out that the patient with true athetosis can generally show no improvement without relaxation.

---

2. McIntire, J. T.: The Incidence of Feeble-Mindedness in the Cerebral Palsied, Proc. Am. A. Ment. Deficiency **43**:44-50, 1938; Cerebral Palsy Treatment Experiment, Crippled Child **20**:94-96, 1942.

3. Phelps, W. M.: Rehabilitation of Cerebral Palsy, South. M. J. **34**:770-776, 1941.

Authorities do not agree on the method for inducing relaxation. It seems not pertinent at this time to discuss the various opinions as to the advisability of hydrotherapy, heat, massage or medication. All agree that voluntary relaxation should be achieved as far as possible,[4]

With very young children, relaxation is sometimes hard to teach because the child may think he is being played with and so may become excited. To avoid such misunderstanding in some cases, the place for play and the place for training should be separate and not interchangeable in their use. In general, relaxation is more easily achieved if the child is lying down; however, in certain cases—for instance those of adolescents—it may be better taught when the patient sits at ease in his chair. Comfortable room temperature and the exclusion of outside stimuli are essential. A blindfold and cotton ear plugs will often help the athetoid relax. Carlson [5] also mentions having the child read the teacher's lips, having him talk while writing and having him speak near a lighted candle, endeavoring to keep the flame slanted away from him, as devices for defocusing attention from his speech and so inducing more relaxed speech. It has been noted that conversational speech by certain athetoid children is much better if carried on while the child's hands are busy with blocks, needlework or games. Quiet, rhythmic music may be used to advantage with some children. Relaxation of speech organs cannot be induced until there is general relaxation. When it has been achieved, special exercises should be given for those muscles which are used in speech. Relaxation may be encouraged by gently tapping the face, neck and shoulders; by rolling the head from side to side, and by grasping the chin and shaking it gently.

The following exercises have been found effective in speech muscle relaxation:

1. In time with music or on four counts, let the head fall forward; to the left; back, and to the right.
2. Yawn.
3. Frown; relax.
4. Close the eyes tightly; allow them to open gently.
5. Open the eyes wide; allow them to close gently.
6. Round and protrude the lips; relax.
7. Smile broadly with the lips closed; relax.
8. Open the mouth, and with no force exhale a prolonged "ah."

Other exercises may be arranged according to Jacobson's principles.[4] "Relaxation—" or "rag-dolls" are very effective with some children.

4. Jacobson, E.: Progressive Relaxation, ed. 2, Chicago, University of Chicago Press, 1938.

5. Carlson, E. R.: Born That Way, New York, John Day Company, 1941, pp. 143-160.

For small children, all exercises should be in the form of games with opportunity for imitation. Much of the ability to relax comes from a feeling of confidence. Since it is necessary that the child carry the relaxation which he has learned in the treatment into his other activities, his teachers should make every effort to see that he keeps his feeling of security.

The relaxation period is followed by exercises for the tongue and lips, with training in chewing, sucking and swallowing. If the child is old enough to be interested in stories, Little Boy (or Girl) Tongue, who lives in a castle with red doors and white doors, can do many interesting and amusing tricks. If the child in question is too young to care about the adventure of Little Boy Tongue, he may enjoy "licking like a kitty" on a lollipop or taking some peanut butter from the roof of his mouth with his tongue. Syrup or jam spread along his lips is an effective device for motivating tongue motions. Eating and speaking movements have a common origin,[6] and progress in the former insures progress in the latter.

In dealing with certain older children, time is saved if the therapist frankly explains what she is trying to teach and enlists the child's cooperation. This method is the most desirable one if the child realizes his need for speech and is old enough to take an active part in his training. In such cases, working in front of a mirror is especially desirable, the patient being asked to perform some of the following motions:

Point tongue outward, upward, downward and to each side.

Rotate the tongue around the outside of the lips.

Touch each tooth with the tip of the tongue.

Alternately protrude and retract the lips.

Say slowly "ah—oo—ee—Q—x" or "wah—way—wee—wi—wo—woo."

Some children react unfavorably to mirror work. If such reaction is observed, the mirror work should be omitted until such time as the child will enjoy and profit by it.

Weak muscles of the lip can be strengthened by exercises using bottle corks. The corks range in size from ½ to 2 inches (1.25 to 5 cm.) in diameter. The child holds the cork in his mouth by closing his lips around it. Therapy is begun by using a size which the child can hold and proceeding from this to sizes which he cannot hold until his lip muscles are stronger.

---

6. Froeschels, E., and Jellinek, A.: Practice of Voice and Speech Therapy, Boston, The Expression Company, 1941, pp. 179-180.

It may be necessary at first for the therapist to assist the weak muscles. Chewing motions are often particularly difficult for the child. He should practice on actual food, yet because of his difficulty the food given him is usually so soft that he cannot chew it, no matter how much he tries. In such cases caramel or taffy candy should be substituted. A rather large, tough but well flavored piece of meat offers good chewing practice. Gum chewing is excellent because it provides an opportunity for continuous chewing and swallowing. Needless to say, the therapist is always watching while such exercises are in progress. The older child can practice chewing imaginary food with his lips closed.

Sucking is encouraged by allowing the child to take his orange juice or eggnog through brightly colored straws. In the same way, pretty, easily handled cups will encourage him to drink. The ability to suck or drink continuously, with swallowing rapid enough to keep the liquid from running out of the child's mouth, is as much a speech goal as phonation or articulation. Once the child understands how to swallow, he can usually eliminate his drooling.

Breathing difficulties are common among children with cerebral palsy. Many spastic patients have true "reversed breathing." In normal breathing, the chest and the abdomen should rise and fall together. In reversed breathing one will rise as the other falls due to a reversal of diaphragmatic movement. This type of breathing can be observed either directly or by placing one light weight object on the chest and another on the abdomen infrasternally.

Athetoid children with severe tension may also have this reversal, but more often than not their breathing follows no predictable pattern.

Before any one should attempt to do corrective work on reversed breathing, he should be thoroughly familiar with the breathing mechanism, and should know what muscles are at fault. Sometimes the breathing is extremely shallow. Even with older children, breathing exercises should be masked by accompanying activities. Some of these activities which encourage breath control without calling the child's attention to his breathing are singing, reciting memorized poems, playing wind instruments, blowing soap bubbles, blowing out candles, blowing on a candle enough to move the flame but not extinguishing it, holding a piece of tissue paper against the wall with the breath stream, blowing a feather but not allowing it to fall, pulling a string from a clown's mouth and vocalizing a prolonged "ah," panting like a dog, and laughing (beginning with a slow "ha-ha-ha" and going faster, until the imitation laugh has turned into a genuine diaphragm-shaking chuckle). An interesting breathing exercise which also aids the muscles of voice production is suggested by Emil Froeschels: "The patient is advised to clench his fists, to raise them to the nipples, to push them down with

great strength, synchronically speaking a vowel, a syllable, shorter and then longer words, and so on." [7]

As has been pointed out, when the athetoid patient learns to relax, many of his articulatory difficulties may be at an end. However, in the case of the spastic patient, while relaxation is helpful, other training must be carried out to correct dysarthic speech. It might be noted in passing, that a person with spastic paralysis generally has the same articulatory difficulty every day and that a person who is with him all the time learns to understand his speech. In athetosis, on the other hand, the speech is variable. At times when the patient is relaxed, his speech may be good, but while he is tense, it may be unintelligible. The methods previously mentioned for defocusing attention may be employed to a good advantage here. Spastic children will not generally outgrow their speech difficulties as so many parents hopefully believe. Corrective training should be instituted at the earliest opportunity, in order that the child may not acquire functional dyslalias in addition to his organic speech disorders.

Articulatory therapy is begun on those sounds which are the most acceptable and proceeds toward those which present the most difficulty for the child. In theory, certain sounds are easier to make than many others; but in the case of children with cerebral palsy this is not always true. Each child must be tested as an individual and have an individual rehabilitation program mapped out for him. Interesting games and devices motivate the child to work. In general, the therapist tries to present the sound by auditory, visual and motokinesthetic stimuli. When the isolated sound is mastered, it must be incorporated into words and these words into sentences. And thereby develops another problem. A child may be able to speak given words correctly, yet when he attempts to carry on a conversation these very words may become unintelligible.

A series of work books may be the means of overcoming this difficulty by presenting the isolated sound, a word which contains it and rhymes or stories in which the word appears. These all may become sources of conversation. This conversation is useful for another reason. Spastic children have monotonous voices with little or no inflection. A story told and retold by the teacher, always with the same words stressed, makes a definite impression on the child, and he will tell it with the same inflections. Thus a conversation about Little Jack Horner may run like this:

Teacher: Here is little Jack Horner. Is he a boy or a girl?

Child: He is a BOY.

7. Froeschels, E.: A Contribution to the Pathology and Therapy Due to Certain Cerebral Lesions, J. Speech Disorders 8:301-320, 1943.

Teacher: Is he a BIG boy or a LITTLE boy?
Child: He is a LITTLE boy.
Teacher: Is he EATING or DRINKING?
Child: He is EATING.
Teacher: Is he eating CAKE or PIE?
Child: He is eating PIE.

In such conversations, the child should not be interrupted for corrections. The teacher notes the errors and corrects them at another time.

Among children with cerebral palsy, frequently there is found a youngster who presents an articulatory problem which is not due to his physical condition except, perhaps, indirectly. The child may use infantile speech because that is the speech his parents use in speaking to him and he knows no other. Another reverts to infantile speech when ill, although avoiding it normally. Still another child mispronounces words because he learned to talk in a community where a foreign dialect is used.

If a child persists in an error, it may be because he does not correctly hear the sound. The audiogram made at the time of his speech diagnosis should be studied to see if it indicates any defect in hearing which might cause him to be unable to make the desired sound. This hearing test should be frequently repeated. Weather conditions, extraneous noises and the child's physical and mental state at the time of the test influence the results and thus make retesting necessary in order to have an accurate picture. The child who is hard of hearing can be benefited by a hearing aid and should wear one, not only in speech class but wherever he can do so. At first the child may not enjoy the hearing aid, but as he learns to use it the advantages will overcome his dislike. His teacher should help him learn to hear. The picture or object is presented, and the teacher names it. The child sees the word formed at the same time that he receives the auditory stimulus through his hearing aid. He may also be given motokinesthetic stimuli as the therapist assists the muscles of the lips and the tongue to form the word pattern. If the hearing aid is not available, or until it is, the visual and motokinesthetic methods can be used.

In athetoid children, especially in those with a severe involvement of the upper extremities, there is sometimes a central deafness for certain tones, usually the high ones. This defect in hearing may go unnoticed, because these children tend to become lip readers and their speech defects are often erroneously attributed to other causes.

Many children with cerebral palsy have no speech at all. Since it has been said that in this discussion educability is assumed, one of the

reasons for delayed speech—mental deficiency—will not be considered. Other reasons may be:

1. The child does not want to talk. Many parents are so anxious to do all they can for their afflicted child that they anticipate his every wish.

2. No one talks to him. When the child does not begin to talk at the usual age for speech to be established, his family may fall into the error of ignoring him and not talking to him.

3. He has no social contacts. No boys and girls come to play, and he goes nowhere. Hence he misses the stimuli which the normal child gets.

4. He may be aphasic. The aphasia, which is caused by a brain lesion, may appear in one of several forms. For example, the child may be able to read words but not to say them.

5. He may be deaf or hard of hearing.

6. Spasticity or athetosis or both may prevent the functioning of the speech organs.

The earliest speech training is begun by teaching the child to babble—that is, to make the sounds which a normal child usually makes before he begins actual speech. The therapist may assist the child by manipulating the child's lips, at the same time making the desired sound. It is well to remember that the child with cerebral palsy does not know how to do the things that normal children learn by the simple process of maturation. There is an optimum time for the acquisition of each pattern of development, and the child can be taught that pattern with much more success near the time when normal children learn it. Hence, speech training should be instituted as early as possible.[8]

Speech is acquired by unconscious as well as by conscious imitation. Toy animals on parade serve as motivation for animal sounds; the sounds of trains, airplanes, busses, cars and vacuum cleaners, all may be imitated. Many children will "sing" before they will talk. Children like nursery rhymes and singing games. Conversation about toys and pictures should contain simple words—often repeated—which are in a child's daily life. Also conversation about articles of clothing, friends and food should be used. In talking about food, chewing movements may be started. For example, the teacher shows a picture of an apple. She says, "M-m-m, what a good apple. Have a bite?". She offers the child a make-believe bite of the apple. He accepts it, and they both chew in great enjoyment.

8. Stinchfield, S. M., and Young, E. H.: Children with Delayed and Defective Speech, Stanford University, Calif., Stanford University Press, 1938.

It is of greatest importance in the child's first speech that he vocalize, and of less importance that every sound be correct. Correction is achieved as the therapist repeats the word correctly and assists the child's muscles to form the desired pattern.

Various group or communal activities are introduced in the speech work at a cerebral palsy center, all with the idea of helping the child to gain a place in society and to feel a sense of personal worth. Some of these activities are choral speaking, singing, rhythmic exercises to music and the memorizing and reciting of poetry. Even babies soon learn to recite. A picture of a cow is shown. The therapist begins: "The friendly——." "Cow," says the child, to complete the phrase, and so on through the poem. Other activities are story telling, work books (made as bright and attractive as possible), speech games and laughing games.

There are certain items of equipment necessary for the speech room. Among these items should be listed: (1) a couch and pillows, (2) mirrors large enough for the therapist and the child to see each other at the same time, (3) a hand mirror, (4) tongue depressors, (5) tissue handkerchiefs, (6) gauze, (7) towels, (8) sandbags, (9) a table, (10) chairs and (11) a cupboard or bookcase.

Other items which make the therapy more interesting and effective are: 1. A record player and records. These are used for relaxation, coordination, rhythm and speech motivation. 2. A mirrophone or a permanent recording machine. The latter instrument is useful in letting a child hear his own speech. However, one should be watchful to guard against any undesirable psychologic effect which might follow when the child realizes that his speech is unintelligible. Most children are fascinated by the recording machine and like to work with it. 3. Rag dolls. These are used to teach relaxation and to motivate speech. 4. Animals of wood, pottery or cloth. They are used to motivate beginning speech. Also, they usually have their tongues out—which prompts little boys and girls to do likewise. 5. Pictures of children yawning, blowing bubbles, dressing themselves and singing. 6. Bubble pipes. 7. Whistles. 8. Lollipops. 9. A jar of peanut butter. 10. A play table with blocks and pegs. 11. A toy xylophone. This is excellent for accompanying "Rock a Bye Baby." 12. A toy telephone. 13. A big "sailor boy" face with a string in his mouth to teach breath control. 14. A blackboard. 15. A bulletin board. 16. Games. 17. Story and picture books. 18. Candles and matches.

In a center for patients with cerebral palsy there are children of all ages and with all degrees of handicaps. Each has his own personality and need. The therapist must realize this and thus be ready to offer a new activity if this particular child does not respond to the therapy which is being used.

Speech rehabilitation is carried on most efficiently when it is coordinated with other therapy. By means of physical therapy, the child's weak muscles are strengthened and the hypertense ones relaxed. Better breathing is established. As he becomes more able to do things physically, his speech tends to improve. Occupational therapy teaches self help in dressing, feeding and recreation, all of which increases his sense of personal worth. There is a definite, mutually beneficial, relationship existing between speech therapy and school work. As the child's speech improves, he likes school better. The more he enjoys school, the better opportunity he has to find some field of interest in the learning situation in which he can make a good showing and so gain the feeling of confidence which produces better speech. Pediatricians, neurologists, orthopedists, orthodontists, oculists and otolaryngologists form the medical foundation on which speech therapy in the child with cerebral palsy must be built if it is to be most valuable and permanent.

CONVULSIONS IN CHILDHOOD

Twenty Year Study of 2,500 Cases

M. G. PETERMAN, M.D.
MILWAUKEE

THIS report is concerned with the clinical study of 2,500 children with convulsions who have been seen in a private office and in hospital practice over a period of twenty years. It does not include a large series of patients seen in a large clinic previously, whose cases were reported elsewhere, nor does it include patients seen in homes or in outlying hospitals where facilities and circumstances did not permit adequate studies to establish completely satisfactory diagnoses. The first 1,000 cases of the present series have been reported and have formed the basis for the first classification of convulsions in childhood to be presented in the literature.[1] This study has been presented in many centers, and it was illustrated with the first moving picture film

TABLE 1.—*Causes of Convulsions in Two Thousand Five Hundred Cases (Total Series)*

Cause	Per Cent
Acute infection	33.4
Idiopathic epilepsy	26.3
Cerebral birth injury or residue	14.2
Miscellaneous causes	13.1
Infantile tetany	7.4
Cause not established	5.6

depicting the clinical features of the various types of convulsions.[2] The clinical value of this study has been amply established. The reliability of the classification is attested by the striking correlation between the results in the first 1,000 cases and the results in the additional 1,500 cases herein recorded.

Table 1 presents the causes of convulsions in the entire series of 2,500 cases. It may be noted that in one third of the cases the cause of convulsions was due to or associated with acute infections. This includes generalized acute infections and the onset of the acute infectious diseases. In one fourth of the cases the symptom was due to idiopathic, or essential, epilepsy. In 14 per cent of the cases evidence was presented

1. Peterman, M. G.: Convulsions in Childhood, J. A. M. A. **102**:1729 (May 26) 1934.

2. Peterman, M. G.: Convulsions in Childhood, J. A. M. A. **99**:546 (Aug. 13) 1932.

showing that cerebral birth injury or the residual thereof was the cause of convulsions. In 5.6 per cent of the cases the basic cause could not be established. The rationale of my original classification of the convulsive diseases into certain age groups has been substantiated by the continued studies. As stated previously, there are certain age periods when specific diseases are most prevalent. These diseases

TABLE 2.—*Convulsions in Newborn Babies and Those of Ages up to One Month (Seven per Cent of Total)*

Cause	Cases
Cerebral birth injury	122
Acute infection	18
Hydrocephalus	6
Idiopathic epilepsy	6
Infantile tetany	5
Meningitis	3
Uremia	1
Cerebral agenesis	1
Congenital heart disease	1
Congenital syphilis	1
Cause not established	12

TABLE 3.—*Convulsions in Infants from One to Six Months (12.9 per Cent of Total)*

Cause	Cases
Acute infection	102
Infantile tetany	61
Cerebral birth injury residue	59
Cerebral agenesis	18
Idiopathic epilepsy	15
Meningitis	10
Hydrocephalus	6
Pertussis (cerebral hemorrhage)	2
Cranial injury	2
Subdural hematoma	1
Congenital syphilis	1
Polioencephalitis (Strümpell)	1
Cerebral thrombosis	1
Congenital heart disease	1
Cause not established	43

produce or precipitate convulsions and thus account for the incidences designated. Tables 2 to 6 inclusive reveal this information (ages at the time of the first convulsion).

Seven per cent of the convulsions occur within the first month of life. Most of these are due to cerebral birth injury. Thirteen per cent of the convulsions appear in the age period of 1 to 6 months. Most of these are due to acute infections. The convulsive age of childhood is the period between 6 and 36 months. This interval accounts for 47 per cent of the total cases. It is the age period when acute infections

are most prevalent and serious. These are responsible for most of the convulsions. However, epilepsy also makes its first major appearance. The first convulsive manifestations of the residual of birth injuries

TABLE 4.—*Convulsions in Infants from Six to Thirty-Six Months of Age (47.2 per Cent of Total)*

Cause	Cases
Acute infection	554
Idiopathic epilepsy	197
Cerebral birth injury residue	123
Infantile tetany	120
Meningitis	37
Encephalitis, acute and chronic	26
Cerebral agenesis	15
Brain injury, traumatic	11
Pertussis (with cerebral hemorrhage)	8
Polioencephalomyelitis	7
Hydrocephalus	6
Subdural hematoma	4
Nephritis, acute	2
Transfusion reaction	2
Anesthesia	2
Congenital syphilis	2
Hemophilia (with cerebral hemorrhage)	1
Cerebral thrombosis	1
Schilder's disease	1
Gastroenteritis (intracranial sinus thrombosis?)	1
Congenital heart disease	1
Intracranial vascular lesion	1
Cause not established	56

TABLE 5.—*Convulsions in Children from Three to Ten Years Old (27.4 per Cent of Total)*

Cause	Cases
Epilepsy	332
Acute infection	158
Cerebral birth injury residue	48
Encephalitis, acute and chronic	33
Post-traumatic	23
Meningitis	12
Cerebral agenesis	9
Brain tumor	9
Tetanus	6
Nephritis, acute	5
Insulin shock	5
Lead encephalopathy	3
Congenital heart disease	2
Hydrocephalus	2
Congenital syphilis	2
Uremia	2
Subdural hematoma	1
Postanesthetic	1
Hemangioma (cerebral)	1
Gastroenteritis (intracranial sinus thrombosis?)	1
Cerebral edema (nephrosis)	1
Pertussis	1
Malaria	1
Cause not established	27

are prominent. This is also the age when tetany is most prevalent. Between 3 and 10 years of age 27 per cent of convulsions make their first appearance, and epilepsy becomes the major cause. Acute infections are still responsible for over 23 per cent of the cases. From 10 to 15 years of age only 6 per cent of the patients have their first

convulsion. Epilepsy is responsible for most of these. These tables provide a useful and practical guide for the diagnosis and further study of the convulsive syndrome in childhood.

The studies of artificially induced convulsions in man and in animals have shed little light on the mechanism of the convulsive state. Mechanical or chemical excitation of the normal brain does not reproduce the syndrome found in clinical disease. Postmortem studies of brains have provided little information on the cause of the convulsive state, even in patients who have died in status convulsus.[3] The outstanding contribution to the study of convulsions has been Berger's introduction of the electroencephalograph.[4] With this remarkable apparatus one is now able to establish the diagnosis of epilepsy, to classify the various types and even to diagnose the case of the potential

TABLE 6.—*Convulsions in Children from Ten to Sixteen Years (5.9 per Cent of Total)*

Cause	Cases
Idiopathic epilepsy	107
Encephalitis, acute and chronic	8
Congenital syphilis	5
Cerebral birth injury residue	4
Nephritis, acute	3
Post-traumatic	3
Tetanus	3
Cerebral agenesis	3
Acute infection	2
Meningitis	2
Toxemia (burn)	1
Henoch's purpura	1
Hemangioma of face and brain (Lindau's syndrome)	1
Cerebral hemorrhage (scurvy)	1
Cause not established	2

epileptic before he has had a seizure (chart 1). It is also of great assistance in localizing brain tumors,[5] in classifying behavior disorders and in evaluating treatment in the convulsive state.[6] The electroencephalogram has been included in the office study of these patients since August 1941. It has become an indispensable aid in diagnosis and prognosis. The electroencephalogram has also been of inestimable value in the study of siblings for potential epilepsy and in the determination of the possibility of recurrence in the patient who has had convulsions in infancy or in the remote past. A number of children with a history of periodically recurrent behavior disturbances, temper spasms and "bad nightmares" have been found to have abnormal electrograms indicating a convulsive state or epilepsy (chart 2). Of course, the

3. Peterman, M. G., and Glaser, K.: Fatal Status Epilepticus, Am. J. Dis. Child. **68**:122 (Aug.) 1944.

4. Berger, H.: Arch. f. Psychiat. **87**:527, 1929.

5. Jasper, H. H., and Nichols, I. C.: Am. J. Psychiat. **94**:835 (Jan.) 1938.

6. Logan, G. B.: Proc. Staff Meet., Mayo Clin. **17**:345 (June 3) 1942.

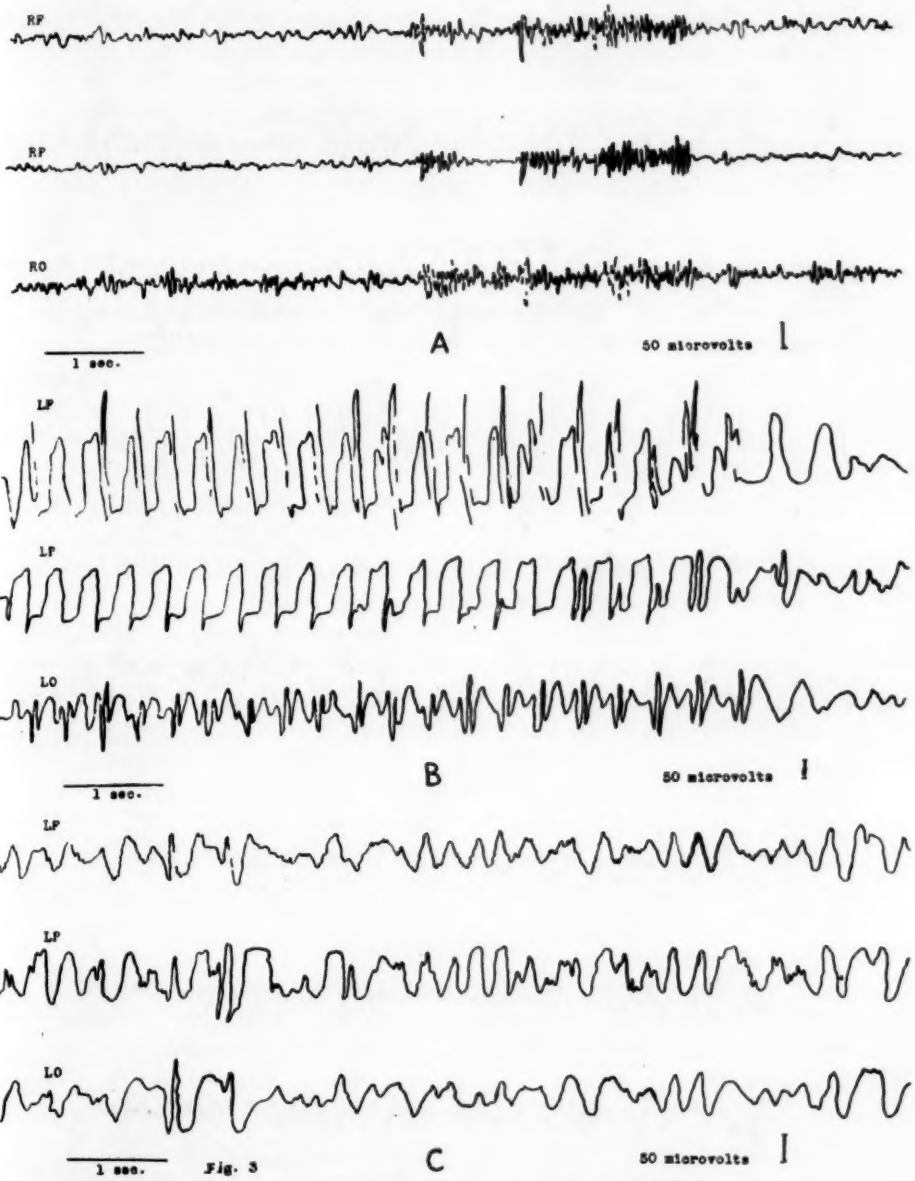

Chart 1.—*A*, F. J., 8 years old with grand mal epilepsy. Recurrent rapid dysrhythmia in all three leads. *B*, N. Z., 12 years old, with petit mal epilepsy. An episode of recurrent three per second spike waves and delta rhythm. *C*, L. H., 3 years old. Extensive cortical (birth) injury with convulsions. Scattered spikes and slow waves.

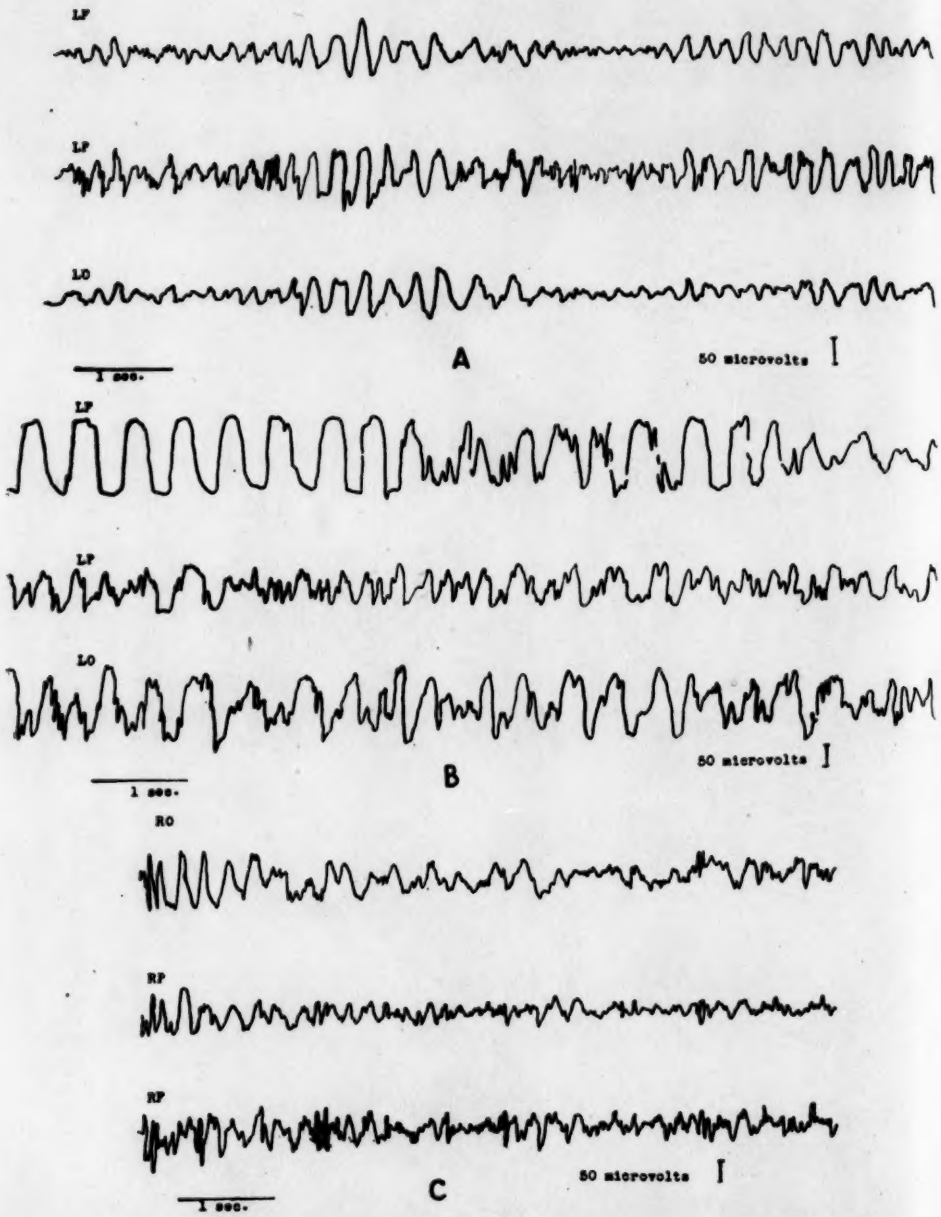

Chart 2.—*A*, J. G., 5 years old, with recurrent severe "nightmares." Recurrent three and four per second slow waves of delta rhythm. *B*, J. H., aged 18 years. Psychomotor phase, with one per second high, flat spikes in boy with petit mal who was free of all seizures for four years. *C*, D. D., aged 2 years, 4 months. One convulsion at 11 months and four at 2 years, only with high fever. Tracing shows, the three per second high spikes and spike waves of epilepsy.

electroencephalogram is not infallible nor has the interpretation reached the status of the electrocardiogram. A reliable apparatus and a competent technician are essential for the production of satisfactory electrograms. The value and interpretation of the tracing are entirely dependent on the ability and experience of the analyst. The younger the child, the greater are the technical difficulties in obtaining a satisfactory tracing. It is often necessary to make several tracings at intervals to obtain a period of cerebral arrhythmia. Complete relaxation, preferably sleep, is necessary.

ACUTE INFECTIONS

It is common knowledge that acute infections or high fevers induce or precipitate the largest number of convulsions. The mechanism of this reaction remains to be solved. It is my opinion that infections or fevers precipitate convulsions only in those children who have a potential convulsive state.[6a] Most of these children have a convulsion threshold or a temperature level beyond which the seizure is precipitated. Most children admitted to a hospital have fever, and yet only 1.9 per cent of those admitted to the Milwaukee Children's Hospital are subject to convulsions. Even this figure is weighted because of the disproportionately large number of children admitted for study of the convulsive state. Children with cerebral injuries, potential tetany or potential epilepsy require a combination of circumstances to set off the trigger mechanism of the convulsive state. For instance, the alkalosis resulting from hyperventilation will often precipitate petit mal seizures.[7] This mechanism does not apply to chemical irritants or toxins which act directly on nerve cells. Thirty-one children with a history of convulsions precipitated by or associated only with fever were studied. The electroencephalograms helped to establish the diagnosis for 24. Sixteen of them were found to have epilepsy; 6 had slight cerebral birth injury residues, and 2, chronic encephalitis.

EPILEPSY

Idiopathic epilepsy is the most common cause of recurring convulsions in childhood. The electroencephalograms of patients, parents and siblings have established the earlier clinical observation [8] that this disease is inherited as a mendelian recessive. Berger's electroencephalograph has also established the fact that there must be an organic cerebral defect to produce a characteristic cerebral dysrhythmia. The typical electroencephalograms of petit mal, the variants of petit mal, the psychomotor equivalent and grand mal epilepsy confirm the con-

6a. Buchanan, D. N.: M. Clin. North America **30**:163 (Jan.) 1946.

7. Rosett, J.: Brain **47**:293 (Aug.) 1924.

8. Peterman, M. G.: Epilepsy in Childhood, Am. J. Dis. Child. **32**:416 (Sept.) 1926.

tention that essential epilepsy is a distinct disease entity and not merely a manifestation of the convulsive state.[9] The terminology is of no consequence. The attempt to relegate essential epilepsy from a disease entity to another manifestation of the convulsive state[10] is futile and would hinder the study of the disease.

Making the diagnosis of essential epilepsy and the differential diagnosis distinguishing it from the other causes of the convulsive state is usually not difficult.[11] A family history of convulsions, a normal birth history, absence of preceding cerebral accidents and lack of complications of infectious disease provide a clear background for diagnosing the condition of the otherwise normal child in whom convulsions progressively increasing in frequency and severity develop. The usually suggestive description of an aura or a cry or of abnormal behavior followed by a tonic, then a clonic, spasm, succeeded by a loss of consciousness or a confused mental state, sometimes accompanied with involuntary micturition or defecation, all followed by drowsiness or deep sleep, completes a picture recognized by even the laity. Between seizures in the early stage of epilepsy the child is normal, and his intelligence level compares favorably with that of his siblings.[12] The results of physical and neurologic examinations are normal. A dietary indiscretion or a gastrointestinal disorder usually precedes or precipitates the seizure.[13] The ancient practice of purging and fasting was well founded and remains good treatment.[14] The diagnosis must be made by exclusion to eliminate the other causes of convulsions specified. Spinal punctures, blood chemistry studies, etc., are best accomplished in a hospital. Making of an electroencephalogram is then in order to confirm the diagnosis. Barring this, if it is not available, the results of treatment provide further confirmation of the clinical impression.

CEREBRAL INJURY

Under this heading are included all prenatal injuries such as occur in prematurity, in a prolonged second stage of labor, after excessive maternal anesthesia or sedation (particularly with administration of morphine, paraldehyde, scopolamine, the barbiturates, nitrous oxide and ether), after natal injuries such as breech deliveries and traumatizing instrumentation and after postnatal injuries such as anoxia, chilling,

9. Peterman, M. G.: Illinois M. J. **84**:306 (Nov.) 1943.

10. Peterman, M. G.: Wisconsin M. J. **43**:708 (July) 1944.

11. Panel Discussion on Convulsions, American chapter, International League Against Epilepsy, Chicago, May 8, 1939.

12. Peterman, M. G.: Wisconsin M. J. **41**:1001 (Nov.) 1942.

13. Peterman, M. G.: J. Pediat. **17**:114 (July) 1940.

14. Hippocrates, in Tempkin, O.: The Falling Sickness, Baltimore, Johns Hopkins Press, 1945.

severe anemia and infection.[15] Erythroblastosis or Rh incompatibility with its resultant anemia, jaundice or kernicterus may produce a pathologic cerebral condition before, during or after delivery.[16] An adequate history together with a careful examination and follow-up study will establish this causative factor.

These patients usually present a history of difficulties beginning shortly after birth with feeding problems, excessive crying, delayed development, mental retardation, spasticity or flaccidity, incoordination and paraplegia.

The remaining causes of convulsions do not require discussion. This series includes 5 cases of tetany in the newborn and 181 cases of infantile tetany which conform to the well known picture. The latter group are characterized by increased irritability, carpopedal spasm, signs of rickets and positive Trousseau and Lust signs. There are usually low calcium and increased phosphorus values in the blood serum.

It will be noted that my series of 2,500 cases does not include instances of convulsions associated with hypoglycemia. My criteria for this diagnosis include:

1. A consistently low blood sugar level (below 60 mg.) before or during a convulsion, with an elevated blood sugar content after the seizure.

2. A flat or abnormally low blood sugar curve after the administration of dextrose.

3. Initiation of a convulsive seizure by prolonged fasting or the injection of insulin.

4. Termination of the convulsive seizure by the administration or injection of dextrose or of epinephrine to raise the blood sugar level to normal.

5. A normal electroencephalogram between seizures.

A fasting blood sugar determination has been made on all of the children in this series. Repeated determinations have been made when there was a suspicion that the convulsions were due to hypoglycemia. Sugar tolerance curves have been made in these cases and in those in which the patients had a fasting blood sugar level below 60 mg. per hundred cubic centimeters. The criteria just enumerated have been applied to all cases in which hypoglycemia was suspected or in which a diagnosis of hypoglycemia (or hyperinsulinism) had been made elsewhere. No case has met these requirements. Conditions diagnosed elsewhere as due to hypoglycemia have been established as essential

15. Schreiber, F.: J. Pediat. **16**:297 (March) 1940.

16. Yannet, H., and Lieberman, R.: Central Nervous System Complications Associated with Kernicterus, J. A. M. A. **130**:335 (Feb. 9) 1946.

epilepsy. A number of children with temporary recurrent hypoglycemia have been found, but these have never evinced more than collapse, weak spells or fainting spells without convulsions or loss of consciousness.

TREATMENT

The acute or precipitate convulsion requires diagnosis more than treatment. Most convulsive seizures have completed their episode before medical treatment becomes available. The greatest danger lies in a continuation of the seizure until status convulsus results. Caution must be exercised to avoid doing more harm than good. First of all, morphine or opium derivatives must never be used. These drugs depress the respiratory center and the cough reflex, they decrease peristalsis and they mask diagnostic signs and symptoms. Secondly, hot baths are contraindicated. More children have been burned than helped by hot applications.

The simplest, most effective and safest treatment for the control of a convulsive seizure is the administration of chloroform or vinyl ether by inhalation. These anesthetics should be kept fresh and available wherever convulsions are anticipated. They are most effective in the convulsions of epilepsy. Since one third of the convulsions have developed because the body temperature has passed the convulsive threshold, hydrotherapy and antipyretics are the *sine qua non* of treatment. Cool sponges, ice packs, ice bags and cool enemas should be used until antipyretics may be administered and until they have reduced the body temperature to near normal. In the event of an acute disease of the respiratory tract the anesthetics should not be used except in extreme emergency. Phenobarbital or sodium phenobarbital and amytal preparations are next in order, even after the convulsion has subsided. Persistent seizures or status convulsus is best treated with tribromethanol (avertin), 75 mg. per kilogram by rectal instillation.

If epilepsy is suspected or diagnosed and the previously mentioned anesthetics are not available, magnesium sulfate may be administered by mouth, by rectum, intramuscularly or, in an emergency, by vein. When the convulsion is prolonged or associated with cyanosis, oxygen should be administered by inhalation to prevent cerebral damage from anoxia. The bowels should be evacuated by catharsis and enemas.

The prolonged treatment of epilepsy will not be discussed in detail here.[17] Suffice it to say that the ketogenic diet remains the most effective treatment available for petit mal seizures.[18] Until the intro-

17. Peterman, M. G.; Litchfield, H. R., and Dembo, L. H.: Therapy of Infancy and Childhood, Philadelphia, F. A. Davis Company, 1942.

18. Brennemann, J.: Practice of Pediatrics, Hagerstown, Md., W. F. Prior Company, Inc., 1945, vol. 4, chap. 12. Peterman.[20]

duction of "Tridione" (3,5,5-trimethyloxazolidine-2,4-dione) no drug produced any therapeutic effect in this disease. Treatment with the new drug has been reported as having controlled petit mal in two thirds of 30 cases in which it was used.[19] I have used "Tridione" in 12 cases. In pure petit mal the results have been excellent. In cases of associated, potential or known grand mal, however, this drug has precipitated the most severe major convulsions experienced by the patients treated. The drug should be useful as a diagnostic agent to precipitate suspected grand mal seizures. This drug may seriously depress the bone marrow. Most children with petit mal seizures also have active or potential grand mal attacks. For these patients the ketogenic diet offers the greatest promise of results.[20]

Phenobarbital remains the most effective, the least harmful and the least expensive drug available for the treatment of major seizures. It produces the lowest incidence of undesirable side effects. This conclusion is based on twenty-five years of experience with all of the anticonvulsive drugs available. The various preparations of phenobarbital under trade names are no more effective than the standard drug. Diphenylhydantoin sodium is sometimes effective in patients who have not responded satisfactorily to phenobarbital, but the undesirable side effects are frequently disturbing.

The treatment of infantile tetany resolves itself into a matter of the administration of calcium. This is best accomplished by giving calcium chloride by mouth or intravenously. This drug may be given orally in a 10 per cent solution in elixir of glycerrhiza. Intravenously, calcium chloride in a 5 or 10 per cent solution should be injected slowly.

CONCLUSIONS

The determination of the cause of a convulsion depends primarily (and sometimes finally) on the history and the description of the seizure. The electroencephalogram offers the sole means of establishing the diagnosis by objective proof. Without this aid it may be necessary to continue the study by the process of exclusion. A therapeutic trial provides further aid in diagnosis.

The tables furnish a useful guide to the common causes of convulsions in children. One third of the seizures are due to or precipitated by fever. Most of these children have a basic potential convulsive state which is usually epilepsy. The fever and its associated disturbances provide the trigger mechanism which initiates the convulsive episode.

---

19. Lennox, W. G.: The Petit Mal Epilepsies, J. A. M. A. **129**:1069 (Dec. 15). 1945. Wolff, E., and Peterman, M. G., in discussion on Lennox, p. 1074.

20. Peterman, M. G.: Treatment of Epilepsy, J. A. M. A. **130**:966 (April 6) 1946.

Recurrent convulsions are usually due to epilepsy. The diagnosis of this disease and the results of treatment are best evaluated by means of the electrogram. "Tridione" (3,5,5-trimethyloxazolidine-2,4-dione) may prove to be a useful drug in the treatment of pure petit mal epilepsy. It is useful as a therapeutic aid, if necessary, to precipitate potential grand mal seizures. However, it is a dangerous drug.[21] The ketogenic diet is the most effective and safest treatment available for all epilepsy in children. Phenobarbital remains the drug of choice in the treatment of grand mal epilepsy. The most effective immediate treatment of a convulsion in an emergency is inhalation of chloroform or of vinyl ether.

411 East Mason Street.

21. Harrison, F. F.; Johnson, R. D., and Ayer, D.: Fatal Aplastic Anemia Following Use of Tridione and A Hydration, J. A. M. A. **132**:11 (Sept. 7) 1946. MacKay, R. P., and Gottstein, W. K.: Aplastic Anemia and Agranulocytosis Following Tridione, ibid. **132**:13 (Sept. 7) 1946.

Case Reports

FRACTURE WITH OSTEOMYELITIS OF THE MANDIBLE IN A NEWBORN INFANT

EDWIN P. SCOTT, M.D., and C. C. ROTONDO, M.D.
LOUISVILLE, KY.

OSTEOMYELITIS of the superior maxilla in the newborn infant is uncommon, while osteomyelitis of the mandible is extremely rare.

Wilensky [1] (1932) reviewed the literature of osteomyelitis in infants and suggested that it be separated from the general subject of osteomyelitis because it is more or less a definite clinical entity. His communication dealt with acute osteomyelitis of the jaws, both upper and lower, which occurred most commonly in the first weeks or months of life. The cause was generally considered to be bacterial, the organisms being staphylococci, streptococci and coliform bacilli. The sources of the infecting organisms were listed as: (1) the vaginal canal of the mother; (2) the fingers of the accoucheur or the nurse; (3) the nipples and breasts of the mother, and (4) the fingers or apparatus used in cleansing the baby's mouth after birth. The question of the mechanism by which the infection is introduced (blood stream or primary lesion) is still unsettled. The majority of observers favor the latter.

Turner [2] (1942) reported a case of a newborn infant who had osteomyelitis of the superior maxilla. When the infant was 17 days old, an abscess was noted in the right side of the upper gum, and four days later a molar tooth was removed from this site. Treatment consisted of the administration of sulfathiazole. During the following week seven other teeth were pushed out of the upper jaw. At the age of 26 days pus began to exude from the right mandible. This discharge stopped within five days. At the age of 4 months a swelling at the angle of the lower jaw on the right side broke down and drained into the mouth and extruded small spicules of bone and tooth buds. At the same time the infection spread to the left side, where a swelling developed over the ramus of the left mandible. When the infant was last seen, at the age of 6 months, all fistulas had closed except the one in the right side of the upper jaw.

From the Department of Pediatrics, University of Louisville School of Medicine, services of Dr. James W. Bruce and Dr. W. W. Nicholson.

1. Wilensky, A. O.: Osteomyelitis of the Jaws in Nurslings and Infants, Ann. Surg. **95**:33-45, 1932.

2. Turner, J. H.: Osteomyelitis of the Maxilla and Mandible in a Newborn Infant Due to Staphylococcus Aureus, Arch. Pediat. **59**:1-4, 1942.

Ehrenfest [3] (1940) in discussing injuries to the newborn infant stated: "The severest injuries in the infant's mouth are produced in connection with the Mauriceau-Veit-Smellie method of delivery of the after coming head. If one or two fingers introduced into the mouth are improperly used for strong traction the resulting lesions vary anywhere between mere laceration of the skin in the corner of the lips to complete evulsion of the lower jaw, including fracture of the lower jaw. . . ."

It is believed that the following case is of sufficient rarity to be recorded in the medical literature.

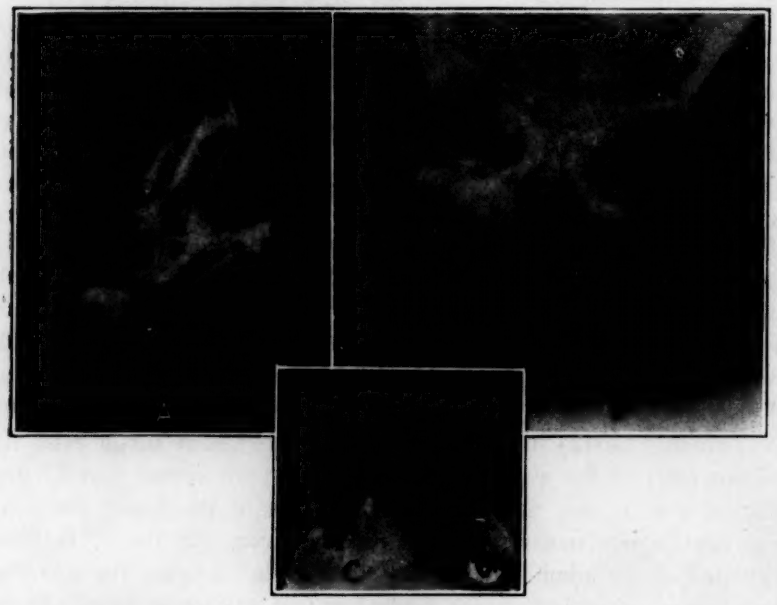

Fig. 1.—Roentgenograms of the mandible (*A, B* and *C*) revealing a fracture and ragged destruction at the symphysis.

REPORT OF A CASE

This 2 week old white girl was admitted to the Children's Free Hospital April 3, 1945 with the chief complaint, as given by the mother, of "drainage from the jaw." The mother stated that soon after delivery she had noticed a hard bluish area over the lower jaw. . The mother was assured that the condition was due to the hard delivery and that it would disappear. However, the traumatic site gradually became larger and softer, and six days prior to admission to the hospital it began to discharge purulent material.

During the prenatal period the mother suffered from toxemia of pregnancy. She was 17 years of age and unmarried; the father was 23 years of age and well. There were no previous pregnancies. The birth weight was 3 pounds and 6 ounces

3. Ehrenfest, H., in Davis, C. H.: Gynecology and Obstetrics, Hagerstown, Md., W. F. Prior Company, Inc., 1940, vol. 2, chap. 6, p. 31.

(1,477 Gm.), and the delivery was described as a difficult breech extraction.[4] Feedings consisted of evaporated milk, water and 5 per cent carbohydrate.

Physical examination of the infant on admission to the hospital revealed a poorly nourished white girl, who appeared acutely ill. There was a small draining sinus in the center of the lower jaw, and the surrounding area was slightly indurated.

Fig. 2.—Photograph showing the loss of several deciduous teeth.

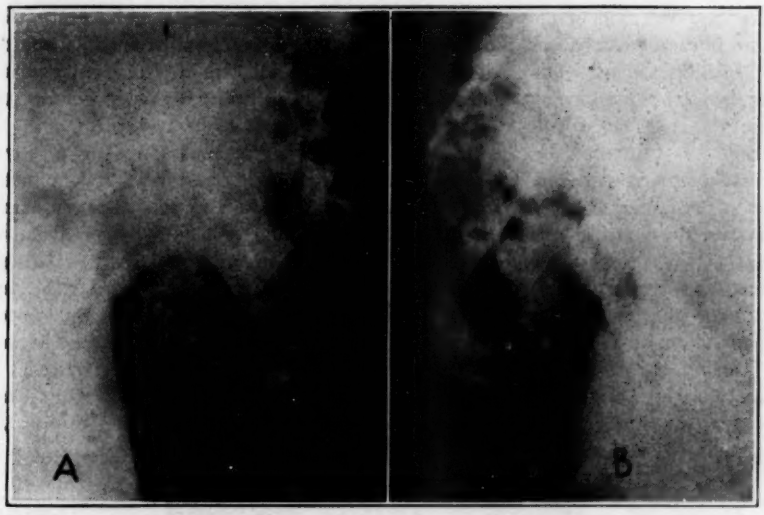

Fig. 3.—*A*, a roentgenogram made June 1, 1945 showing slight osseous regeneration and *B*, one on June 19 showing the presence of considerable new bone.

4. It was later learned that the delivery was performed by an alien posing as a physician in a small rural hospital in Kentucky, a fact which probably explains the trauma during delivery, with the resulting fracture and osteomyelitis of the mandible.

There were rales in the chest bilaterally. The weight was 4½ pounds (2,041 Gm.). The clinical impression on admission was that the infant had osteomyelitis of the lower jaw and bronchopneumonia.

Laboratory Data.—The red blood cell count was 4,200,000 per cubic millimeter, with a hemoglobin content of 17 Gm. per hundred cubic centimeters; the white blood cell count was 18,100 per cubic millimeter, with polymorphonuclear leukocytes 38 per cent and lymphocytes 62 per cent. The urine revealed a trace of albumin but was otherwise not remarkable. The result of the Kahn test of the blood was doubtful at first, but a negative reaction was reported ten days later. Purulent material collected from the draining sinus revealed Bacillus coli on culture, and culture of the blood showed nonhemolytic streptococci. Roentgenograms of the mandible (see fig. 1 *A*, *B* and *C*) [5] revealed a fracture and ragged destruction of the mandible at the symphysis with a defect about 5 mm. in width.

Course and Treatment.—The infant was immediately given penicillin, a dose of 5,000 units every three hours intramuscularly. A powdered milk formula (60 cc.) was given every three hours by gavage, but owing to diarrhea this was changed the following day to boiled skimmed milk. On April 6 administration of sodium sulfadiazine was started, 3 cc. of a 5 per cent solution, every eight hours subcutaneously. Body hydration was maintained with transfusions of whole blood and plasma and with hypodermoclyses.

One week after admission the diarrhea was somewhat under control and 5 per cent carbohydrate was added to the formula. At this time the infant lost several deciduous teeth (fig. 2). On April 12 the route of administration of sulfadiazine was changed to the oral route, 0.125 Gm. every six hours. Three days later the amount of penicillin given was reduced to 2,500 units every three hours intramuscularly, and the draining sinus was irrigated with a 1:500 solution of penicillin sodium. On April 23 the use of sulfadiazine was discontinued, and five days later the intramuscular administration of penicillin was stopped. At this time the red blood cell count was 3,100,000 per cubic millimeter and the hemoglobin content 9 Gm. per hundred cubic centimeters. On May 2 a new episode of diarrhea began, which was adequately treated by starvation, administration of sulfadiazine, transfusions of blood and plasma and subcutaneous administration of dextrose and saline solution. On May 8 the discharge from the sinus in the lower jaw had ceased; hence irrigation with penicillin was discontinued and cauterization with 10 per cent silver nitrate was begun. A roentgenogram of the mandible made on June 1 (fig. 3 *A*) revealed slight osseous regeneration, and on June 19 (fig. 3 *B*) there was considerable new bone present.

During the last month of hospitalization there were two more episodes of diarrhea, which were treated as in the previous infection. The sinus of the lower mandible gradually closed, and the infant was discharged on June 29 weighing 8 pounds (3,742 Gm.)

CONCLUSION

Recovery was brought about in a newborn premature infant with fracture and osteomyelitis of the mandible.

5. The roentgenograms were read by Dr. H. L. Townsend.

Progress in Pediatrics

RECURRENCE OF INFECTION FOLLOWING THERAPY WITH SULFONAMIDE COMPOUNDS AND PENICILLIN

PHILLIP E. ROTHMAN, M.D.
LOS ANGELES

THE PRINCIPAL clinical handicap in the use of penicillin and the sulfonamide compounds is the inability to determine the duration of treatment necessary to eradicate an infection. This difficulty is due to the rapid disappearance of all clinical evidence of the disease before a cure has been completed. The so-called masking of symptoms is responsible for the premature discontinuance of medication. Recurrences of infection result not infrequently, and two or three courses of treatment may be required before recovery finally ensues. Spink and Hall [1] emphasized that this problem creates two potential dangers, namely, that an infection may be controlled but not eradicated and that drug-resistant strains of organisms may develop and may be disseminated. In the treatment of mild infections of the respiratory tract, lymphadenitis and low grade cutaneous infections with cellulitis, a relapse represents more of an annoyance to the patient than a matter of serious import, as the ultimate prognosis is almost invariably good. Much more grave are the relapses of the meningitic disorders, in which the early cessation of treatment may prove a contributory factor in the production of permanent damage to the brain and the cranial nerves. A recent case in point reported by Labby,[2] of recurrent pneumococcic meningitis following treatment with sulfonamide compounds, is that of a man in whom a mild degree of hydrocephalus developed. This patient had many recurrences, and the dilatation of the ventricles was interpreted as due to a chronic arachnoiditis from the long-standing infection. Incompletely treated venereal infections constitute a complicated public health problem. This applies particularly to the treatment of gonorrhea by a single injection of penicillin. In discussing subacute bacterial endocarditis, Bloomfield and Halpern [3] have remarked:

1. Spink, W. W., and Hall, W. H.: Penicillin Therapy at the University of Minnesota Hospitals: 1942-1944, Ann. Int. Med. **22**:510 (April) 1945.

2. Labby, D. H.: Recurrent Pneumococcic Meningitis Following Sulfonamide Therapy, J. A. M. A. **127**:981 (April 14) 1945.

3. Bloomfield, A. L., and Halpern, R. M.: The Penicillin Treatment of Subacute Bacterial Endocarditis, J. A. M. A. **129**:1135 (Dec. 22) 1945.

"The proposal to treat for a shorter time and then to give more penicillin in case of a relapse does not seem sound to us, since whatever ground was gained by initial inadequate therapy may have been completely lost by the time relapse is evident. Indeed, one may actually be in a worse position since the infecting streptococci may have developed increased resistance to penicillin when subcurative doses are given."

An additional danger in incompletely treated infections lies in the obliteration of the old familiar landmarks that enabled the physician to determine the point at which a patient passed beyond the jurisdiction of medical care and into the realm where surgical intervention was necessary. This is well illustrated in cases of mastoiditis. Extension of a simple otitis media to a mastoiditis requiring surgical treatment may occur while the physician is lulled into a false sense of security by absence of pain, a normal temperature curve and a normal white cell count. Absence of chills, of fever and of a positive blood culture may obscure the presence of sinus thrombosis. The imminence of tragic complications is often evident only after the drug has been discontinued. Weinstein and Atherton [4] have reported a case of acute suppurative otitis media in which a sinus phlebitis occurred during therapy with penicillin. There were no clinical signs of mastoiditis before the surgical procedure was carried out and no evidence of infection of the mastoid bone at operation. It is also obvious that all gradations of symptoms may exist, depending on the daily dosage of the drug prescribed. This particular therapeutic problem was emphasized by Herrell,[5] who stated: "It is necessary to bear in mind, however, the masking effect of penicillin in these cases and exceeding caution is required to avoid becoming too assured of good final results when the striking symptomatic response has been secured. Such premature assurance may permit an infection of low grade, but which requires surgical intervention, to develop into a dangerous infection. The masking effect of penicillin, just mentioned, is similar to, if not more pronounced than, that exerted by the sulfonamides. Frequent roentgenographic studies of the mastoid cells, therefore, are essential parts of the treatment of mastoiditis with penicillin."

An excellent example of the remarkable properties of the drug to mask symptoms is contained in the report of a case of acute appendicitis by Lieutenant C. M. Riley [6] in the *Atlantic Fleet Medical News:*

An 18 year old seaman reported at sick call, having had vague abdominal pain for about twenty-four hours and anorexia, but no frank nausea or vomiting. On

4. Weinstein, L., and Atherton, H. B.: The Treatment of Acute Suppurative Otitis Media with Penicillin, J. A. M. A. **129**:503 (Oct. 13) 1945.

5. Herrell, W. E.: Penicillin and Other Antibiotic Agents, Philadelphia, W. B. Saunders Company, 1945, p. 168.

6. Riley, C. M.: Atlantic Fleet M. News Letter, Dec. 10, 1944, no. 12-44.

examination he was found to have slight rigidity of the rectus muscle on the right side and tenderness directly over McBurney's point, as well as rebound tenderness referred to this area. There was moderate generalized tenderness high in the rectum. The temperature was 100.4 F. and the white blood cell count 14,700. A diagnosis of acute appendicitis was made. Because of the unsatisfactory conditions for operating aboard an old destroyer, medical treatment was selected. He was given sulfadiazine, 4 Gm. immediately, followed in four hours by 2 Gm., with 1 Gm. every four hours thereafter. The large initial doses were given in an effort to produce a high blood level rapidly. Six hours after the first dose physical findings were unchanged but the temperature had fallen to 99.6 F. and the white cell count was 11,000. The next day the temperature remained normal and he began to have a little appetite. Significant physical findings at this time were limited to a diffuse abdominal tenderness. On the third day the ship made port, and the patient was transferred to the hospital. At the time of admission the examining physician could find no signs of acute appendicitis, but he agreed to operate on the basis of the characteristic history. Operation was performed approximately seventy-six hours after the beginning of treatment. The appendix was found to be retrocecal; its tip was extremely swollen and engorged but not gangrenous, and the lumen contained fluid which appeared to be purulent.

In commenting on the case Lieutenant Riley made the following summary: "Despite the symptomatic and laboratory evidence of improvement in this case of acute appendicitis during a seventy-six hour period of full sulfadiazine dosage, the appendix on removal appeared to be in a highly dangerous state. From the therapeutic point of view this would suggest that in medically treated cases of this condition it would be well to continue chemotherapy longer than is indicated by the clinical course."

It is impossible to estimate the frequency of relapses in the treatment of various diseases. Appelbaum and Nelson [7] reported 7 instances of relapse in 67 cases of pneumococcic meningitis in which there was treatment with both penicillin and the sulfonamide compounds. Weinstein and Atherton [4] reported 8 recurrences in 50 cases of acute suppurative otitis media in which penicillin was used. Relapse is rarely encountered in meningococcic infection because of the extreme sensitivity of the organism both to the sulfonamide compounds and to penicillin. In 165 cases of meningococcic meningitis Meyer [8] treated the patients with sulfadiazine plus in some instances meningococcic antitoxin, with only one relapse. The incidence of relapse in ambulatory patients seen in private practice is unquestionably higher than in hospitalized patients, who enjoy the benefit of more careful supervision. If a second or third course of treatment completely eliminates an infection, one may assume that a prolongation of the initial treatment

7. Appelbaum, E., and Nelson, J.: Penicillin in the Treatment of Pneumococcic Meningitis, J. A. M. A. **128**:778 (July 14) 1945.

8. Meyer, A. H.: Meningococcus Meningitis: Report on One Hundred and Sixty-Five Cases, Ann. Int. Med. **22**:543 (April) 1945.

with sufficient dosage will produce a cure. It is desirable, therefore, to search for evidence of persistent infection in patients undergoing treatment in order to guide the duration of administration of the drug to a satisfactory conclusion.

Bacteriologic procedures are helpful but have many limitations. Following the administration of these drugs, the causative organism, as a rule, cannot be isolated from the mucous membranes of the nose and throat in disorders of the upper respiratory tract. Since the organisms often reappear after use of the drug has been discontinued, it is obvious that this period of "cultural latency" is no criterion of a cure. Moreover, the presence of a positive culture would not necessarily signify that a cure had not been effected but might well suggest the possibility of a convalescent carrier. One of the recurrences in Labby's case showed all the clinical and laboratory evidence of the disease, with over 5,000 cells in the spinal fluid, but no organisms were seen and none grew on culture. A blood culture which does not yield the organism may be obtained in many cases of bacteremia twenty-four to seventy-two hours after the institution of treatment with no assurance that a cure has been accomplished. All such studies merely suggest that the drugs act chiefly as bacteriostatic agents.

It has been established by all observers that a normal temperature, pulse rate and respiratory rate may rapidly follow treatment despite the presence of infection. Variations in temperature may often prove most confusing in the interpretation of the patient's status. Not only are the sulfonamide compounds capable of inducing fever, but it has recently been postulated that prolonged fever in cases of subacute bacterial endocarditis when the patients have been treated with penicillin may not necessarily indicate persistent infection or reactions to penicillin or penicillin impurities but may be due to disintegration and absorption of large vegetations. The usual tendency toward a disappearance of eosinophils at the height of a severe infection and their reappearance with the patient's improvement is a sign of no value in determining persistent infection, for there is often sufficient improvement from the use of the drugs to permit an increase in the number of these cells despite the failure of a complete cure. Penicillin does possess an advantage over the sulfonamide compounds in the interpretation of a progressive anemia. When penicillin is used, the anemia may be attributed to the infection whereas the sulfonamide compounds per se may cause alterations in the red cell count and the hemoglobin. A recent case illustrates this advantage.

A girl aged 2 years was hospitalized on the seventh day of an acute suppurative otitis media because of an abrupt elevation of temperature. Myringotomy had been performed on the second day of illness, and a thick purulent discharge persisted. No clinical evidence of mastoid involvement was apparent. The white

cell count was 14,400 and the red cell count 3,720,000. She received 20,000 units of penicillin every three hours for five days. The temperature at no time exceeded 100 F.; the discharge diminished in amount, she played comfortably in bed; she ate well and showed general improvement. After four days of treatment, the white cell count was 8,250 and the red cell count had dropped to 2,930,000. Roentgenograms showed no evidence of osseous destruction. Because of the progressive anemia and the fact that slight pain could now be elicited on direct pressure over the mastoid, a mastoid infection requiring surgical intervention was suspected on the fifth day of treatment. The drug was discontinued, and forty-eight hours later the temperature rose to 101.5 F., accompanied with severe pain and the appearance of edema over the mastoid. Operation revealed both a subperiosteal abscess and perisinus abscess.

It is unfortunate that the most delicate test available, namely the sedimentation test, may show a lag of several days to a few weeks before the results return to a normal level after clinical evidence of the termination of an infection. Consequently an elevation of the sedimentation rate during a symptom-free period cannot be interpreted as a basis for additional chemotherapy. Occasionally a normal sedimentation rate may not be obtained until one month has elapsed following the acute phase of pneumonia, and a lag of two months has been reported after clinical recovery from severe septicemia.

In the absence of a laboratory test for persistent infection, the knowledge necessary to determine the duration of treatment must rest on clinical experience. As the result of observations by a large number of investigators information is now available that will guide therapy in the majority of cases. For example, it is generally believed that treatment with the sulfonamide compounds for meningococcic meningitis may safely be discontinued five days after the spinal fluid becomes sterile and clinical symptoms subside, while with other pyogenic meningitides treatment should be continued for a longer time and preferably for a minimum of two weeks after the patient is asymptomatic. Similar facts have been established for many types of infections, although exceptions to the rule occasionally appear. As the methods of administration and the optimum daily dosage of the drugs in a variety of disorders become clarified, relapses will diminish in frequency. Nevertheless there are factors in each case which resist therapeutic standardization. The principal obstacle is the variation in the sensitivity of the organisms not only in the same epidemic but in the same patient from day to day and week to week. Some workers believe this is due to the rapid disappearance of the drug-sensitive organisms and to a numerical increase in the members of the bacterial colonies which were originally resistant. In respect to penicillin, one is confronted with additional possibilities to explain the occasional lack of therapeutic response. Subcurative doses may result from the variable rate at which the drug disappears from the blood and from the variation

in effectiveness of the natural species of penicillin. Moreover, the possibility of the development and dissemination of resistant organisms by the use of prophylactic sulfonamide compounds, penicillin and sulfonamide nose drops, penicillin troches, gum containing sulfonamide compounds and penicillin aerosol may increase the difficulties that arise in attempting to eradicate infections. More experience is necessary for a complete understanding of the full significance of all factors responsible for relapses.

3875 Wilshire Boulevard.

Abstracts from Current Literature

Biochemistry, Bacteriology, and Pathology

A Study of Sulfapyridine Resistance in Pneumococci. Sophie Spicer, J. Bact. **50**:23 (July) 1945.

The phenomenon of resistance to sulfonamide compounds by different strains of bacteria is not well understood. The results of experiments conducted by the author in connection with resistance to sulfapyridine by pneumococci offer a simple and plausible explanation of what, in general, takes place in a bacterial population on exposure to the action of the drugs. It is considered that resistance or susceptibility to a drug is an inherent characteristic of individual bacterial cells. Relatively resistant and relatively susceptible organisms may exist in the same culture. Susceptible cells on exposure to the drug may either die or be inhibited from multiplying, the surviving cells resuming growth when the drug is discontinued or when the culture is transplanted in normal culture mediums. Resistant organisms, being able to withstand the action of the drug, multiply and in time may constitute the entire bacterial population. The degree of resistance or of susceptibility of a culture depends on the relative numbers of each type present in the culture.

Stoesser, Minneapolis, Minn.

The Effect of Triethylene Glycol Vapor on Air-Borne Beta Hemolytic Streptococci in Hospital Wards. Theodore T. Puck, Morton Hamburger Jr., O. H. Robertson and Valerie Hurst, J. Infect. Dis. **76**:225 (May-June) 1945.

1. The introduction of triethylene glycol vapor into the air plus the application of measures of controlling dust to the floors and bedclothes in the wards for patients with streptococcic sore throat resulted in a reduction in the number of air-borne beta hemolytic streptococci of 93 per cent when the wards were quiet and of 97 per cent during bed-making periods.

2. The dust prevention treatment by itself lowered the streptococcic count by 86 per cent during bed making but not at all when the ward was quiet. However, when the triethylene glycol vapor was introduced into a ward in which dust prevention was already in effect there resulted a further pronounced reduction of the residual streptococci present in the air during both quiet periods and bed-making periods.

3. Concentrations of the vapor maintained at a level just below the fogging point were found to be as effective as supersaturated atmospheres.

4. The apparent reduction in counts of bacteria in the air registered by settling plates was always lower than that recorded by the samplers in which air is drawn through broth. This discrepancy is probably due to the fact that settling plates collect a disproportionately large number of bacteria attached to heavy particles. Such micro-organisms are less susceptible to the killing action of glycol vapor than those borne on small particles.

5. The authors believe that the combination of triethylene glycol vapor plus dust-preventive treatment of floors and bedclothes offers a promising means of controlling air-borne infection in hospital wards.

Toomey, Cleveland.

Metabolism; Infant Feeding; Milk and Other Foods

NORMAL VALUES OF THE ALKALINE RESERVE IN THE NURSING CHILD. MARIO V. DEL CARRIL, ALFREDO LANGRISA, MARCELO CORI and JUAN D. VIDAL, Arq. de pediat. **15**:29 (Jan.) 1943.

These authors found that when the Van Slyke and Cullen method is used for children 1 to 24 months old the medium value of the alkaline reserve of plasma is 51.5 Gm. and that the physiologic borderline limits are 46 and 57 per cent of carbon dioxide.

LOZOYA, Mexico, D. F., Mexico.

SODIUM CHLORIDE CIRCULATION IN PEDIATRICS: ITS CLINICAL IMPORTANCE. SYLVAIN LIPPMANN, Ann. pædiat. **161**:145 (Sept.-Oct.) 1943.

After an introductory discussion of the factors influencing sodium chloride circulation and sodium chloride reaction, the sodium chloride overloading test is explained in a series of cases, observed at the Children's hospital of the University of Zurich, Switzerland.

With a far reaching consideration of the physiologic sodium chloride metabolism, a uniform method is worked out by which rules generally available can be established for the norm. The sodium chloride overloading test has proved a most valuable help for diagnosing and investigating the pathogenesis of diseases in which a disturbed sodium chloride metabolism has been proved. Among them, diabetes insipidus, diabetes insipidus occultus, diabetes salinus renalis Fanconi and fevers of noninfectious origin are specially dealt with. In cases of vegetative diathesis and in troubles with adiposity, disturbances in sodium chloride metabolism are revealed and give an idea of the pathology of the regulation of metabolism, emphasizing the dominating part of the diencephalohypophysial system. Some investigations of patients with nephritis are devoted to the study of the partial function of the chlorine secretion. The process of pathologic transmineralization in cases of diabetes mellitus, pneumonia, icterus and other diseases is clearly shown by means of the sodium chloride overloading test.

AUTHOR'S ABSTRACT.

RETRACTION OF MILK CURD AFTER COAGULATION. ALBERT GYR, Ann. pædiat. **163**: 314 (Dec.) 1944.

The experiments reported show that retraction of the curd is as dependent on the fermentation process and its influence as on the coagulation of the milk itself.

With stronger concentration of the ferment and increased acidity, the following retraction is speeded up but not strengthened.

Warming of the curdling ferment above the optimal temperature before curdling delays the commencement of retraction along with the coagulation process.

The addition of calcium and its withdrawal before curdling delay subsequent retraction. Increase of temperature after coagulation during the course of retraction greatly accelerates the retraction. Above 70 F., after initial acceleration of retraction there is a slight secondary swelling.

There is the question: In what way does the retraction depend on the enzymatic process? The experiments may be best interpreted by stating that retraction must proceed more slowly on any disturbance of the process of fermentation, since it is dependent on the completeness of the coagulation, which itself is governed by the process of fermentation. If complete coagulation is achieved, then retraction takes place as a purely colloidal chemical process analogous to the interpretation of the retraction of the coagulum.

AUTHOR'S ABSTRACT.

STUDY OF THE QUANTITATIVE SECRETION OF BREAST MILK. LADEGAARD PETERSEN, Ugesk. f. læger **106**:773, 1944.

The secretion of breast milk in mothers who had a sufficient amount of milk for their babies did not increase if both breasts instead of one were given at each

meal. If both breasts were given at each meal to infants of mothers with hypogalactia, the secretion of breast milk increased as compared with the condition when only one breast was given at each meal. If the amount of breast milk was 250 Gm. or more when this treatment was started, it was possible to give only the mother's milk in 80 per cent of the cases, and if the amount of breast milk was less than 250 Gm., the secretion of breast milk became sufficient in 40 per cent of the cases. The variations in the secretion of breast milk at different meals were rather large, in mothers with hypogalactia and small in mothers having a sufficient amount of breast milk.

WALLGREN, Stockholm, Sweden.

Vitamins; Avitaminoses

STUDIES ON THE GROWTH AND DEVELOPMENT OF MALE CHILDREN RECEIVING EVAPORATED MILK: II. PHYSICAL GROWTH, DENTITION, AND INTELLIGENCE OF WHITE AND NEGRO CHILDREN THROUGH THE FIRST FOUR YEARS AS INFLUENCED BY VITAMIN SUPPLEMENTS. TERESA FOLIN RHOADS, MILTON RAPOPORT, RUTH KENNEDY and JOSEPH STOKES JR., J. Pediat. **26**:415 (May) 1945.

White and Negro children from low income families, who received evaporated milk as the sole milk supply from birth through 5 years of age, were observed at periodic visits to the clinic of the Children's Hospital of Philadelphia. They were divided into groups in order to allow comparisons of two levels of vitamin D, (1) that amount provided by customary feedings of irradiated evaporated milk containing 135 U. S. P. units per reconstituted quart and (2) 1,500 units in cod liver oil (1 tablespoonful), and to determine the effect of supplementation of the diet with vitamin A and with vitamin B complex.

Group 1, as controls, received irradiated evaporated milk as the sole antirachitic. Group 2 received nonirradiated evaporated milk plus 1 tablespoon of cod liver oil daily, containing approximately 1,500 units of vitamin D and 15,000 U. S. P. units of vitamin A. Group 3 received irradiated evaporated milk plus 10 drops of carotene daily, equivalent approximately to 2,250 U. S. P. units of vitamin A. Group 4 received irradiated evaporated milk plus 10 drops of carotene and ½ tablespoon of brewer's yeast. The brewer's yeast furnished approximately 0.5 mg. of vitamin B_1 and 0.2 mg. riboflavin.

A suggestive difference in the hemoglobin level appeared at 6 months of age in favor of the yeast-fed group. Mean serum protein levels of all groups remained within normal limits. The variation in the vitamin D intake as well as the supplementation with vitamin A and with vitamin B complex was shown to be without consistent effect on such developmental observations as age at the closing of the anterior fontanel, age at standing with support, age at standing without support, age at walking alone and age at eruption of teeth.

Measurement of the intelligence quotients at 3 years of age revealed no differences between groups. A low and almost equal incidence of mild roentgenographic osseous changes, not diagnostic of rickets, was found after 2 years of age at both levels of administration of vitamin D.

The incidence of dental caries in all groups was low. This study may indicate the importance of a continuous source of vitamin D during this age period as a factor in reducing the incidence of caries.

Racial comparisons revealed significant differences between white and Negro children in the proportions of the body. The Negro children had serum protein values significantly higher than the white children at 1, 2 and 3 years of age. The Negro children had a lower incidence of dental caries. That they had a slightly lower mean intelligence quotient than the white was accounted for, in the main, by the less skilled occupational groups from which the Negro children were drawn as compared with the white children.

AUTHORS' ABSTRACT.

Acute Contagious Diseases

PURPURA FOLLOWING SCARLET FEVER. W. J. MORROW, Arch. Pediat. **62**:255 (June) 1945.

A fatal case of purpura which appeared ten days after the onset of scarlet fever is presented. Thrombopenia was demonstrated. Observations at autopsy are given, including the observation of hyperplastic megakaryocytes in the bone marrow.

GRULEE, JR., Minneapolis.

RUBELLA AND CONGENITAL MALFORMATIONS. EDITORIAL, Internat. M. Digest **46**:50 (Jan.) 1945.

In this editorial, attention is called to several reports in the literature of congenital malformations occurring in infants born of mothers who had rubella during pregnancy. The malformations are serious, occurring usually in the form of cardiac lesions or ocular lesions, particularly congenital glaucoma with resulting blindness. There have been relatively few published reports, but a number of cases have been observed, and they indicate that the incidence of malformations is close to 100 per cent when the rubella occurs in the early months of pregnancy. The question is raised as to the justification of therapeutic abortions in such cases or in any case of virus disease occurring early in pregnancy.

RATTNER, Chicago [ARCH. DERMAT. & SYPH.].

THE NEUTRALIZATION OF POLIOMYELITIS VIRUS BY DOG SERUMS. F. B. GORDON, J. Infect. Dis. **76**:202 (May-June) 1945.

Three of 37 dog serums collected after the 1943 epidemic of poliomyelitis in Chicago were found to neutralize the Lansing mouse-adapted poliomyelitis virus. No neutralization was obtained with serums of 2 chickens and 6 pigeons from the immediate vicinity of a patient with poliomyelitis.

TOOMEY, Cleveland.

THE WATERHOUSE-FRIDERICHSEN SYNDROME. ALFREDO CEBALLOS, THOMAS V. FRANK and WILLIAM F. SIMPSON JR., J. Pediat. **27**:281 (Sept.) 1945.

A series of 8 cases of this disease observed at the Children's Hospital, Washington, D. C., is summarized and presented, together with a review of the history and literature and a suggested method of treatment. Decided increase in recently reported cases is probably due to more accurate recognition and increased incidence of meningococcic infection.

Observations in the cases under consideration were in accordance with the clinical and pathologic data related in the recent literature. In the series, the average value for age incidence was 44 months, for temperature 104.6 F. and for duration of the illness fifteen hours. Signs and symptoms of acute onset, extreme prostration and shock with purpuric manifestations were present in all cases. Bilateral adrenal hemorrhage was the universal pathologic observation with lymphatic tissue hyperplasia reported in 3 of the cases; laboratory results were variable and included recovery of the meningococcus from both spinal fluid and blood in half of the cases and isolation of the causative organism from a smear of the petechiae in 1 case.

The latest evidence would indicate that the condition is one of overwhelming fulminating meningococcemia producing shock. Probably, the clinical-pathologic picture can be explained by the resulting toxemia.

Except for 8 reported cases of recovery from what was apparently the Waterhouse-Friderichsen syndrome, no form of treatment has been successful. Treatment at present is aimed at combating the bacteremia and controlling and improving the circulatory collapse, with institution of supportive measures. Initial laboratory determinations of blood chemistry values and hematocrit readings are urged as

further clues to the establishment of the diagnosis. Sulfonamide compounds and adrenal cortical extract have been the drugs of choice. The value of penicillin cannot be estimated until sufficient clinical trials have been made. Treatment to be effective must be started early in the course of the disease; this is the prime need for a rapid and accurate diagnosis.

Present usage of the term Waterhouse-Friderichsen syndrome should be confined to those cases exhibiting the fairly typical clinical course and undoubtedly to those patients whose symptoms are confirmed at autopsy.

AUTHORS' ABSTRACT.

PERCUTANEOUS IMMUNIZATION AGAINST DIPHTHERIA. H. VOLLMER and M. E. WEGMAN, J. Pediat. **27**:334 (Oct.) 1945.

A series of 33 children were studied with respect to the ability of percutaneously administered diphtheria toxoid to stimulate immunization. All of the children had been primarily immunized two to five years previously. Eighteen children were treated, and 15 were held for controls. The children who were treated received two inunctions of diphtheria toxoid, equivalent to a total of 160 flocculation units, in an emulsion base, while the controls received inunctions of the emulsion base without the toxoid. Titrations of serum indicated a definite rise in antibody in less than 25 per cent of the treated group and no appreciable change in the controls.

The conclusion is reached that with the method used percutaneous administration of booster doses of diphtheria toxoid is not a practical procedure.

AUTHORS' ABSTRACT.

DIPHTHERIA OF THE LARYNX AND TRACHEOTOMY. K. BERNFELD, Acta otolaryng. orient. **1**:73, 1945.

This paper was read before the Oto-rhinological and Pediatric Society in Jerusalem in 1943. Bernfeld reports 4 cases which he picked out from an experience of fifteen years in order to set forth "what may be expected after tracheotomy has been performed for relief of diphtheria of the larynx." The old diagnostic indecision between tonsillitis and diphtheria seems to have been again a puzzle. The author thinks it questionable whether "the diphtheritic nature of tonsillitis can be established in the absence of positive bacterial findings." He says that this cannot be confirmed in some cases until one performs tracheotomy and cultures material removed from the lower airways. In any kind of "stridor," therefore, he advises antidiphtheritic treatment "even if occasionally the bacterial findings may later be negative." In the United States this has been the rule, one assumes, for many, many years. To do less is to subject the child to the risk of fatality, which is inexcusable and, one may say, criminal.

VOORHEES, New York [ARCH. OTOLARYNG.].

Acute Infectious Diseases

NODULES IN RHEUMATIC FEVER. R. H. HARVEY, Arch. Pediat. **62**:302 (July) 1945.

Harvey presents a description of rheumatic nodules and a review of literature pertaining to their cause and clinical significance in rheumatic fever.

C. G. BRULEE JR., Minneapolis.

INFLUENZA: METHOD OF STUDY AND CONTROL. THOMAS FRANCIS, Bull. New York Acad. Med. **21**:337 (July) 1945.

This is a condensation of the recent literature on experimental and clinical work in influenza. Studies until three years ago were limited largely to the bacteriologic phases of the disease and the influence of the virus on animal tissue.

Whether the disease in its sporadic, endemic or epidemic form in man is the same as that produced experimentally in animals is a question open to argument.

There have been many valuable contributions on the nature of the influenzal virus recently and, with the knowledge thus gained, an improvement, even if only in moderate degree, in methods of control. Work on human volunteers indicates that prophylactic means of prevention by vaccination against influenza is possible. The author warns, however, that this phase has not yet been established and that more work is necessary before attempted immunization can be recommended as a universal procedure.

JAHR, Omaha.

EXPERIENCES WITH RHEUMATIC FEVER IN THE ARMY. IRVING S. WRIGHT, Bull. New York Acad. Med. **21**:419 (Aug.) 1945.

Prior to the war most physicians considered rheumatic fever an endemic disease with sporadic but relatively rare epidemics of minor proportions. It was not considered highly communicable. The major factors in its causation were thought to be malnutrition, poor heating and other problems of the underprivileged classes. In the great majority of cases the disease developed in children and adolescents. Experiences with this disease in the army calls for a radical change in these concepts.

In several areas rheumatic fever has assumed epidemic proportions. These occurrences have been most pronounced in the Rocky Mountain and Central states, which formerly were considered relatively safe. In some barracks rheumatic fever has reached a much higher incidence than would have been anticipated in the group of military age. The oldest patient with a first attack in an Army hospital was 42 years old. Generally speaking, the patients in the military forces represent the cream of our youth. They were not poorly nourished or in poor physical condition at the time of the attack. They were in splendid physical training.

Heavy exercise with resulting fatigue has been frequent but not invariable before onset. Exposure to cold and dampness has appeared to precipitate many attacks, but has not been an invariable factor. Close contact in living quarters has been a most consistent environmental factor. The author believes that rheumatic fever, as it occurs in the Army, is a highly communicable disease complex, which frequently is preceded by an outbreak of infections of the upper respiratory tract. There is evidence that it is an anaphylactic reaction, probably to the streptococci of group A. It may be widespread in its attack on well nourished young men believed to be in excellent physical condition. Fatigue, exposure to cold and dampness and close living quarters are potent factors not only in the spread of the streptococci but in the reducing of resistance to an attack through a lowering of the level of tolerance to the organism. It is for this reason that patients with a previous history of rheumatic fever are especially susceptible to recurrences when exposed to the rigors of military life.

Penicillin and the sulfonamide compounds appear valueless in the treatment of rheumatic fever. Prolonged daily dosage of sulfanilamide does appear to lessen the frequency of recurrences, through a reduction in the incidence of infections of the upper respiratory tract. The use of massive doses of salicylates is discussed.

JAHR, Omaha.

A BACTERIOLOGICAL STUDY OF FIFTY PATIENTS IN THE 1934 MOORABBIN TYPHOID EPIDEMIC. J. C. TOLHURST, GLEN BUCKLE and A. HYAMS, M. J. Australia **1**:510 (May 19) 1945.

In 44 of 50 cases of typhoid diagnoses were by culture of the blood. In 6 of 7 cases tested between the fifteenth and twenty-first days of the disease positive cultures were obtained. The use of two mediums (tryptic broth and Wright's broth), and repeated attempts to cultivate the organisms from the blood are shown to be of value. Excellent results were obtained with Wright's broth containing

trypsin. Comparison of six methods of making cultural examinations of feces demonstrated the superiority of two—namely, direct plating on "Difco" Wilson-Blair medium in series (direct Wilson-Blair method) and enrichment in Leifson's selenite F medium followed by inoculations of Wilson-Blair plates. In agglutination tests the necessity for testing for both H and O agglutinins and for using standard suspensions is stressed. In the serum of many patients (20 of 49 tests) "Vi" (virulence) agglutinins developed in the course of the disease, but few non-carriers retained them in convalescence.

GONCE, Madison, Wis.

PROGNOSIS OF MALARIA IN CHILDREN AND ADULTS WITHOUT SPLEENS. EDWARD MELCHIOR, Ann. pædiat. **161**:105 (Aug.) 1943.

Present day authorities consider the spleen an excellent protective organ against malaria, and, in consequence, the prognosis of malaria in persons without the spleen extremely serious, with a fatal course to be expected in most cases. Two cases of malaria in children after extirpation of the spleen are reported, in which the course of the disease was definitely benign. That this is not a special peculiarity in children, but rather of general import, is shown by 3 observations of adults. The aforementioned hypothesis, as also the practical conclusions drawn therefrom, is untenable.

AUTHOR'S ABSTRACT.

Chronic Infectious Diseases

COMPARATIVE STUDY AND SIGNIFICANCE OF THE TUBERCULIN PATCH AND MANTOUX TESTS IN CHILDREN. HYMAN GOLDSTEIN, J. Pediat. **27**:245 (Sept.) 1945.

The author reports his observations over a five year period of the results of a comparative study of the patch and Mantoux tuberculin tests performed on 1,074 children of both sexes between the ages of 8 months and 14 years. Tables 1, 2 and 3

TABLE 1.—*Children Who Received the Patch Tuberculin Test Only*

Age, Years	Children Tested, Number	Reactions	
		Positive	Negative
1 to 14	112	13 (11.5%)	99 (88.5%)

TABLE 2.—*Children Who Received Both Tests, Patch and Mantoux Tuberculin*

Age	Children Tested, Number	Reactions to Tuberculin		Positive Reactions		
		Positive	Negative	To Patch and Mantoux Tests	To Patch Tests Only	To Mantoux Test Only
8 months to 14 years...	962	104 (10.8%)	858 (89.2%)	96 (92.3%)*	3 (2.9%)	5 (4.8%)

* Of the positive cases.

TABLE 3.—*Children Who Received Both Tests, Mantoux and Patch Tuberculin (Divided Into Three Age Groups)*

Age Groups	Children Tested, Number	Reactions to Tuberculin		Positive Reactions		
		Negative	Positive	To Patch and Mantoux Tests	To Mantoux Tests Only	To Patch Test Only
8 months to 4 years....	297	275 (92.5%)	22 (7.5%)	22 (100%)	0	0
4 to 10 years.....	414	369 (89.1%)	45 (10.9%)	40 (89%)	3 (6.6%)*	2 (4.4%)
10 to 14 years.....	251	214 (85 %)	37 (15 %)	34 (92%)	2 (5.3%)*	1 (2.7%)

* See footnote to table 2.

illustrate the results of this study. One notices from table 3 that 100 per cent of the positive reactors in the youngest group reacted positively to both patch and Mantoux tests. It may be observed also that among the positive reactors in the middle group, 89 per cent reacted positively to both the patch and the Mantoux tuberculin tests, and the children of the older group showed 92 per cent positive reactions to both tuberculin tests. This indicated to the author that the patch test is a reliable test and that it compares well as to accuracy and sensitiveness with the Mantoux tuberculin test on children. It is a safe procedure, easy to apply and practical and economical. Faulty technic may result in focal reactions from the Mantoux injection of tuberculin. It is also unwise to perform tuberculin tests during fever, acute disease or contagion when tuberculosis is suspected. One may strike a negative phase and obtain negative reactions to the tuberculin test in tuberculous children. The patch test is particularly useful for testing infants and children of preschool age as well as older children in a community public health program as a means of detecting a potential community focus of infectivity. The roentgen and laboratory data on the children who had positive reactions to the tuberculin tests in this study revealed normal differential and white blood cell counts except for a slight increase in monocytes in 12 per cent of them. The blood sedimentation tests showed an increased rate of from 15 per cent to 30 per cent in 62 per cent of the children. Roentgenograms of the chest showed calcified areas in the tracheobronchial glands in 40 per cent and increased density shadows along the bronchial tree, more pronounced at the hilus, in 63 per cent of the cases. The author could not find acid-fast bacilli in the sputum, in the gastric contents or in smears taken from the oral-pharyngeal area. There were no significant elevations of temperature. One must consider the age of the child, take a careful case history and study the clinical picture when analyzing the reaction to the tuberculin test. The material for patch tests (Vollmer) may be purchased from the Lederle Laboratories, Inc., New York. The author prepared most of his material for patch tests in the following way: One inch (2.5 cm.) wide adhesive tape was cut into 3 inch (7.5 cm.) strips. On each strip were placed three ½ inch (1.3 cm.) rectangular pieces of white filter paper, ½ inch apart and equidistant from top and bottom. The center square was the control, having no tuberculin on it, while the two end squares were impregnated with undiluted old tuberculin. In the younger child the patch test was applied to the back between the scapulas and in the older child to the biceps. The skin was swabbed first with acetone to remove dirt and fatty particles. Close contact of the tuberculin to the skin must be assured for forty-eight hours, after which the patch is removed. The test area is inspected and again inspected for readings forty-eight hours after the removal of the patch. Reading and recordings of results of the Mantoux tuberculin test were made at twenty-four, forty-eight and seventy-two hours after the intradermal injections.

AUTHOR'S ABSTRACT.

PRECAUTIONS TAKEN AGAINST TUBERCULOSIS IN A STATE SCHOOL. DOROTHY PRICE, Irish J. M. Sc., April, 1945, no. 232, p. 128.

One hundred and seventy-two pupils, 14 to 18 years of age, were given tuberculin tests during an eleven year period. Roentgenograms were made of the chest of 86. Thirty-one had primary infection while in the school, with 1 death. The others are well. In none of these has active tuberculosis developed since they have left the school. In 2 of the patients having negative reactions phthisis developed four to five years after they left the school.

SNELLING, Toronto, Canada.

THORACIC ACTINOMYCOSIS IN A CHILD: RESPONSE TO PENICILLIN. F. ARDEN. M. J. Australia **1**:540 (May 26) 1945.

Thoracic actinomycosis which began in the lungs and secondarily involved the chest wall with abscess formation responded immediately and remarkably to therapy

with penicillin. The penicillin was administered simultaneously by two routes: intramuscularly in doses of 10,000 units every three hours and directly into the abscess cavity in a solution of 500 units per cubic centimeter as a daily injection. The intramuscular injections were continued over a period of fifteen days. After therapy with penicillin was stopped, 10 grains (0.65 Gm.) of sodium iodide was administered three times daily for the next two months. Five months after the cessation of treatment, there had been neither local, roentgenographic nor systemic evidence of recurrence.

GONCE, Madison, Wis.

TUBERCULIN AND TUBERCULIN REACTIONS. P. HAUDUROY, Presse méd. **53**:13 (Jan. 13) 1945.

The author discusses the studies of Calmette, Madsen and Helsted on these subjects. Commercial tuberculin varied so much that standardization had to be done. This is now carried out at the Copenhagen Serologic Institute.

In doing Mantoux tests on known infected subjects, it was observed that 0.01 mg. of the tuberculin elicited a positive reaction in 50 to 68 per cent of the patients and 0.1 mg. for 89 to 97 per cent, while the remainder required the use of 1 mg.

Helsted's results with known reactors are also cited. The reaction to the standard Pirquet test was positive in only 42 per cent, the Mantoux reaction to 0.01 mg. of the tuberculin was positive in 53 per cent, and the reaction to a Pirquet test using tuberculin of triple strength was positive in 65 per cent, while the Mantoux test with 0.1 mg. of tuberculin elicited a positive reaction in 80 per cent and the test with 1 mg. 100 per cent.

DAFFINEE, Melrose, Mass.

TUBERCULOUS MENINGITIS IN A CHILD VACCINATED BY MULTIPLE PUNCTURE METHOD. RUBEN GORLERO BACIGALUPI, Arch. pediat. de Uruguay **16**:545 (Sept.) 1945.

An infant of 22 months died of tuberculous meningitis. There had been brief exposure to tuberculosis at 8 months and at 20 months, and the infant had pertussis at 20 months. The final diagnosis was confirmed by appropriate means. The authors cite this case as an exception to the protection usually conferred by BCG vaccination of the newborn.

PLATOU, New Orleans.

PENICILLIN IN TREATMENT OF CONGENITAL SYPHILIS. J. MENEGHELLO, J. ROSSELOT and O. UNDURRAGA, Rev. chilena de pediat. **16**:784 (Aug.) 1945.

Satisfactory results were observed after the treatment with penicillin of 3 infants under 2 months of age with typical manifest congenital syphilis; the total dosage was 30,000-50,000 units per kilogram of body weight. The authors believe that the administration of penicillin constitutes adequate treatment for such patients and recommend its use "for cases in which all other intensive treatment would be too dangerous."

PLATOU, New Orleans.

WHAT BECOMES OF CHILDREN WITH CONGENITAL SYPHILIS? J. C. SCHIPPERS, Maandschr. v. kindergeneesk. **10**:160 (Jan.) 1941.

The author investigated what had become of 110 children with congenital syphilis who had been nursed in his Children's Clinic from 1908 to 1938. Sixty-nine of these children died (53 in the hospital and 16 elsewhere after a shorter or longer time); the majority did not reach the age of 6 months. The surviving children remained as much as possible under control. Concerning 28 patients who were still alive sufficient data could be obtained. Eight had become completely backward or idiotic; 3 were rather backward and were depending on their families for support. Four women were married, and 1 of them had 2 healthy

children. Six girls and 4 men were self supporting and apparently in good condition; 1 girl was still at school and 2 children did not yet go to school. The author strongly recommends that syphilitic parents should be treated before marriage and that the syphilitic mother should again be treated in the first months of pregnancy.

VAN CREVELD, Amsterdam, The Netherlands.

Diseases of Nose, Throat and Ear

SPEECH REHABILITATION. KATHERINE F. THORN, J. Rehabilitation **12**:31 (March) 1946.

The author gives a general review of the types of disorders found in the speech-corrective field: "There is need for an expanded program of speech correction so that therapy will be available to all who require it. The establishment of recognized clinics such as those which are certified by the American Speech Correction Association would reduce materially the number of unsuspecting people who frequent "quack" institutions.

PALMER, Wichita, Kan.

THE LOCI OF STUTTERINGS IN THE SPEECH SEQUENCE. SPENCER F. BROWN, J. Speech Disorders **10**:181, 1945.

Stutterers were asked to read twice a 1,000 word selection. All of the stutterings of all of the subjects were studied individually and after being classified as mild, moderate and severe, in relation to the phonetic value of grammatic function, position in the sentence and length of the words read. Subjects whose stutterings were classed as mild had almost no stuttering on words which did not have at least one of the four factors just mentioned present. The following conclusions were drawn from the data: 1. The presence of one or more factors was accompanied by a greater relative increase in percentage of stuttering. 2. The presence of each additional factor beyond the first one was accompanied by a fairly constant increase in the relative degree of difficulty. 3. There was a high rank-order correlation between amount of stuttering and degree of presence of the four factors. 4. Only 5.3 per cent of the stutterings recorded could not be accounted for in terms of at least one of the four factors. 5. It is chiefly in terms of these four factors that evaluations are made as to the prominence of each word in the speech sequence. This appears to be true of both stutterers and nonstutterers. 6. It is probable in terms of the foregoing evaluation that the loci of stutterings are to be accounted for. In general, stutterers tend to avoid words which are evaluated as being conspicuous and react therefore with caution, hesitancy, effort, conflict, etc. These reactions are predominantly stuttering as contrasted with normal or nonstuttering speech.

PALMER, Wichita, Kan. [ARCH. OTOLARYNG.]

CONSIDERATIONS ON SULFONAMIDE THERAPY IN OTITIS IN INFANTS. JUAN CARLOS MUNYO and MARIA L. SALDUN DE RODRIGUEZ, Arch. de pediat. d. Uruguay **15**:500 (Sept.) 1944.

The authors emphasize tolerance of infants for sulfonamide compounds and note poor correlation of dosage, blood level and clinical response. In 113 otitic infections among infants, they could not attribute improvement or cure to the chemotherapy employed, though mortality was lowered probably by reducing the incidence of extra-auricular complications.

PLATOU, New Orleans.

LATE CLINICAL AND PHONETIC RESULTS OF THE DEVELOPMENT OF LARYNGEAL PAPILLOMAS IN CHILDREN. WALTHER IMFELD, Pract. oto-rhino-laryn. **5**:54, 1943.

Imfeld reports on postoperative control of laryngeal papillomas in children. These growths are both clinically and phonetically more unfavorable in behavior

than any other benign growths. Those occurring in the first three years of life usually have a graver prognosis, because of more frequent recurrences, than those that occur about puberty, which usually lose their tendency to recur. Many of these patients have shown a permanent injury of speech due to the anatomic extensions and involvements.

PERSKY, Philadelphia. [ARCH. OTOLARYNG.]

INTRACRANIAL COMPLICATIONS OF MIDDLE EAR INFECTIONS. ANNA SCHOENHOLZER, Pract. oto-rhino-laryng. **5**:113 and 194, 1943.

A survey is made of 138 cases of infection of the middle ear in which intracranial complications occurred in the Berne Clinic from 1925 to 1941. The patients represented 7.7 per cent of all patients seen in this clinic. The complications of cases of acute otitis media outnumbered those of cases of chronic otitis media. The discussion includes the symptoms, the therapy and the prognosis. Epidural abscess is the most frequently occurring complication and the most favorable to therapy, since cure was effective in 75 cases. Sinal thrombosis and otitic septicemia occurred in 30 cases, with cure in 66 per cent. In 20 cases otitic meningitis occurred, in all of which it was fatal. In 13 cases abscess of the brain developed, in 7 of which it was cured. The intracranial complications usually occurred by direct extension of the infection from the mastoid process, less frequently by way of the blood vessels, through a dehiscence of bone or by the labyrinthine route. Surgical intervention was always indicated in these cases, and it was supplemented with the administration of massive doses of sulfathiazole or Irgamid (N_1-dimethylacroyl sulfanilamide). If an abscess of the brain was suspected, the particular lobe was punctured, and if evidence was obtained, the lobe was incised, opened widely and drained by means of a suction pump. The after-treatment consisted in draining off the secretions daily.

With the advent of sulfanilamide therapy, the number of complications in recent years has decreased, and the prognosis has improved. However, the prognosis depends on the character of the intracranial complication. It undoubtedly is more favorable with epidural abscess, sinal thrombosis and abscess of the brain. However, the prognosis of otitic meningitis is still extremely grave.

PERSKY, Philadelphia. [ARCH. OTOLARYNG.]

RESIDUAL LYMPHATIC TISSUE IN THE TONSILLAR FOSSAE FOLLOWING TONSILLECTOMY. E. LUSHER, Pract. oto-rhino-laryng. **5**:275, 1943.

At the thirtieth meeting of the Swiss Otorhinolaryngologic Society, held at Aarau, June 26 and 27, 1943, Lusher discussed the role of residual lymphoid tissue in the tonsillar fossae. He made a survey of 224 patients who were tonsillectomized. One year and more after operation residual tissue was found in 104 patients. The site varied from the lower pole to the upper pole, or small masses of tissue were studded throughout the tonsillar fossae. In spite of the presence of this residual tissue, 87 patients did not present any symptoms. On the other hand, 17 had various symptoms, such as pain, acute infection, peritonsillar abscess and focal infection.

The author considers the anatomic basis of the possibility of residual tissue. Sometimes it is due to an extension of the plica triangularis to the base of the tongue, which may or may not have small masses of lymphoid tissue enclosed in its folds. At other times there is a small amount of tissue in the upper pole that was retained in the upper folds. Often small remnants of lymphoid tissue are carried deep into the capsule by repeated tonsillar infections which produce secondary scarring and fibrosis in this capsule, and lastly there may be either breaks or so-called dehiscences in the capsule which permit an extension of lymphoid tissue into the muscular beds. The relative merits of the Sluder method, snaring and electrocoagulation for removal were evaluated. The author believes that the Sluder technic is still the method of choice, although with this method

or with the use of the snare a careful inspection of the fossae must be made in the attempt to remove any residual lymphoid tissue. On the other hand, he questions the advisability of removing the plica triangularis, since the latter affords a certain amount of lymphatic drainage and prevents the dry pharyngitis which is seen occasionally.

PERSKY, Philadelphia. [ARCH. OTOLARYNG.]

Diseases of the Gastrointestinal Tract, Liver and Peritoneum

CONGENITAL DIAPHRAGMATIC HERNIA. EDWARD J. DONOVAN, Ann. Surg. **122**:569 (Oct.) 1945.

Congenital diaphragmatic hernia occurs more often than was formerly suspected. The symptoms may be circulatory, respiratory or gastrointestinal, depending on the herniated structures whose function is interfered with. It is sometimes surprising how few symptoms some patients present. The physical signs in the chest are often so confusing that the diagnosis may be missed if a roentgenogram is not taken.

The author advises that an operation be done as quickly as possible after the diagnosis is made: first, because in cases with a part of either the small or the large intestine in the chest there is grave danger of intestinal obstruction; second, because the abdomen will not develop while the structures are allowed to remain in the chest and when the structures are returned to the abdomen it will be too small to receive them. The author prefers the abdominal approach through a subcostal incision.

Postoperatively all patients should be placed in an oxygen tent and kept there for several days. Fluid requirements should be met by parenteral methods.

Seventeen cases of congenital diaphragmatic hernia in which the patients were operated on are reported.

BANTIN, Omaha.

CONGENITAL DIAPHRAGMATIC HERNIA WITH DESCRIPTION OF A NEW SIGN. H. SHAFIK and H. ABOASY, Arch. Pediat. **62**:285 (July) 1945.

A case of diaphragmatic hernia, diagnosed on physical examination and confirmed by roentgen studies, is presented. The authors describe a sound heard low over the left side of the thorax anteriorly "exactly resembling that of the blow of a motor car trumpet" and suggest the usefulness of this "trumpet sign" in the clinical diagnosis of the anomaly in question. A brief discussion of the possible causation of the sound is given.

GRULEE, JR., Minneapolis.

DIARRHEAL DISEASES IN NEW GUINEA. C. FORTUNE and A. A. FERRIS, M. J. Australia **1**:337 (April 7) 1945.

The authors found the most important cause of diarrhea among troops in New Guinea to be acute bacillary dysentery. Treatment with sulfaguanidine consisted in an initial dose of 7 Gm. followed by 3.5 Gm. five times a day for the first four days and then 3.5 Gm. three times a day for three days. Food was allowed from the onset. For the first four days patients were given the hospital light diet, and from the fifth day onward a general hospital diet with meat, fish and vegetables was allowed. Some patients were given normal army diet from the onset, and there was no noticeable ill effect. No deaths occurred among 2,810 patients treated during eighteen months, and the average period of stay in the hospital in 474 consecutive cases was fifteen days. Diagnosis and bacteriologic cure were established by means of rectal swabs (obtained through a proctoscope) cultured on desoxycholate-citrate agar. Amebic dysentery had a low incidence (3 per cent) and is briefly discussed.

GONCE, Madison, Wis.

Nervous Diseases

HEARING LOSS IN CEREBRAL PALSIED CHILDREN. BERNEICE R. RUTHERFORD, J. Speech Disorders **10**:237, 1945.

One hundred and seventy-five children enrolled at the Dowling School were given audiometric tests. These children were placed in three classes: i. e., those with cerebral palsy, with congenital defects and with acquired defects. In 7 cases the records were discarded as unsatisfactory. In the remaining 168 cases, there were hearing losses of 15 per cent in the entire good speech series and 17 per cent in the entire speech-defective series. The cerebral palsy group was more closely comparable to the congenital physical defect group and to the acquired physical defect group in incidence in hearing loss. In the cerebral palsy group, 14 per cent of the children had severe hearing loss; in the acquired defect group, 11 per cent; and in the congenital defect group, 0.6 per cent. The percentage of persons showing hearing loss was greater in the good speech subgroup with congenital speech defects, 21 per cent; but in the defective speech groups, the percentage of cases showing hearing loss was greater—in the cerebral palsy group, 29 per cent. The incidence of hearing loss was greater in the extrapyramidal defective speech subgroup than in the pyramidal defective speech subgroup of those with cerebral palsy. There seems to be evidence in the reactions of these children handicapped by cerebral palsy that all of the hearing problem is not due to the hearing loss per se, but is part of the larger picture of cerebral palsy.

PALMER, Wichita, Kan.

PNEUMOCOCCIC MENINGOENCEPHALITIS CURED WITH SULFADIAZINE AND PENICILLIN. LÓPEZ CLARES, CALDERÓN and OSORIO, Bol. méd. d. Hosp. inf., México **3**:161 (July) 1945.

The authors begin their article by giving the clinical histories of 2 patients for both of whom the diagnosis of pneumococcic meningoencephalitis was made with the aid of the laboratory.

The first patient was 3 years of age and had remained in the hospital sixty-nine days; during that time, he received 34 Gm. of sulfadiazine, both by the intravenous and by the oral route, plus 12 Gm. that was given previous to his admittance. Also, previously, the patient received, intravenously, 240,000 units of penicillin. In the hospital, 600,000 units more was injected intravenously, intramuscularly and intrathecally. The recovery was uneventful.

The second patient was 1 year and 5 months of age and recovered completely in sixteen days. This patient received 35 Gm. of sulfadiazine and 1,200,000 units of penicillin, which was injected intrathecally and by continuous myoclysis. The recovery was also uneventful.

Due to the dangers of the usual routes, the authors recommend the continuous myoclysis or the ordinary intramuscular route.

MADERO, Mexico, D. F., Mexico.

PRELIMINARY REPORT ON THE TREATMENT OF CHOREA BY THE ELECTRIC SHOCK. LUIZ CERQUEIRA, Pediat. e puéricult., Bahía **13**:95 (Dec.) 1943.

Basing his treatment on the good results obtained by means of pentamethylenetetrazol in the treatment of chorea, the author used the electric shock in a case of chorea, with satisfactory response.

LOZOYA, México D. F., Mexico.

A NEW SYNKINETIC PHENOMENON IN CHILDHOOD—CHIRO-CHREMASTERIC SYNKINESIS. M. SCHACHTER and S. COTTE, Ann. pædiat. **160**:208 (April) 1943.

The authors give a description of a synkinesis between the hand and the cremaster muscle as observed in 100 boys between 5 and 18 years of age. The

compressing of a dynamometer caused the equilateral or contralateral, quick and complete ascension of the testicle. The phenomenon appeared in 57 per cent of all the cases.

AUTHORS' ABSTRACT.

DIFFERENTIAL DIAGNOSIS OF POLYRADICULITIS. PROF. G. FANCONI, H. ZELLWEGER and A. BOTSZTEJN, Ann. pædiat. **162**:59 (Feb.-March) 1944.

In a survey of 14 cases of polyradiculitis the differential diagnostic criteria between polyradiculitis and poliomyelitis are discussed. The polyradiculitis can be mortal, as in the case of Landry paralysis, or it can produce extended but totally reversible pareses, as in the Guillain-Barré "Syndrome" or as a "forme fruste" with a sensation of weakness in the legs, with or without recurrence. All these forms show an albuminocytologic dissociation in the spinal fluid. In 1 case the question of chronic polyradiculitis is raised. There is a discussion of the relations of polyradiculitis to postdiphtheritic polyneuritis, to Feer's disease and to tumors of the brain and spine which are associated with albuminocytologic dissociation.

AUTHORS' ABSTRACT.

Psychology and Psychiatry

DEFINITION OF PSYCHOPATHIC PERSONALITY. HARRY F. DARLING, J. Nev. & Ment. Dis. **101**:121 (Feb.) 1945.

Following a brief yet comprehensive discussion of the etiology, psychopathology, symptomatology and prognosis of the condition generally referred to as psychopathic personality, the author concludes that: It is a mental disease which develops during or before puberty. It is caused by an inherited predisposition or by an acquired personality deviation due to psychic or somatic factors or both; these in turn cause a deficiency in the super-ego, which is characterized by stereotyped deviations in the moral, social, sexual and emotional components of the personality, without intellectual impairment, psychosis or neurosis and with lack of ability to profit by experience. It is of lifelong duration in almost all cases.

JAHR, Omaha.

PSYCHIATRIC EVALUATION OF THE HYPERKINETIC CHILD. W. F. SCHNEIDER, J. Pediat. **26**:559 (June) 1945.

The pediatrician's position is paramount for evaluating the role of the infant or child's physical condition as it contributes wholly or in part to emotional maladjustment according to the author. Some child psychiatrists have stated that approximately 35 per cent of the children's behavior problems have an organic (endogenous) cause. Physical causation should be carefully considered when the pediatrician examines and treats the "hyperkinetic" child.

The hyperkinetic child is described as one who is restless, overactive and aggressive; he has a distractable attention, flightiness of ideas and an impulsive, sometimes explosive motor output. He may have unpredictable, disturbing behavior in school and at home. He is not as violently aggressive, destructive and lacking in judgment as the child with the postencephalitic or post-traumatic behavior disorder. Excluded also in this paper are those children with mental deficiency, birth injuries and cerebral agenesia.

The psychobiologic approach to the evaluation of this behavior problem assumes that there is a clear understanding of the hereditary background, as well as all environmental influences affecting the development and continuance of the problem. Early traumas, such as prenatal, birth and immediately postnatal traumas, severe illnesses and accidents with complications, must be evaluated. Interpersonal relationships, not only in the family but also in the school, church and immediate environment (gang), must be known. The examination of the child entails a searching physical examination stressing aberrations of anthropometric measurements, glandular dyscrasias, evidence of avitaminosis, allergic manifestations,

confused laterality (mixed dominant handedness and eyedness) and general part-dysfunctions (visual and auditory defects and neurologic disturbances). A clear understanding of the child's intellectual capacity enables the physician better to adjust the child's ability to the school and to the parent's demands. Never should the physician underestimate the child's own ability to discuss and often to give considerable insight into his own difficulties. The child should be interviewed alone to promote freedom with the examiner. On this evidence of personality structure can be superimposed further clinical laboratory data (audiograms, ophthalmograms, electroencephalograms) and studies of personality (Rorschach and achievement tests). Slowly we arrive at our picture of the psychobiologic "oneness" of the personality. The pediatrician should realize that in the problem child one or two minor physical deviations may play greater havoc than a major physical disability in a normally adjusted child.

The author gives presentations of cases to elucidate the importance of the physical anomalies which contribute toward hyperkinetic behavior. Cases of children with average to superior intelligence have been discussed as they have favorably responded to alleviation of their physical abnormalities. A bibliography lists references to the current literature which will serve to orient the pediatrician to psychobiologic implications of behavior problems.

AUTHOR'S ABSTRACT.

AVOIDING BEHAVIOR PROBLEMS. BENJAMIN SPOCK, J. Pediat. **27**:363 (Oct.) 1945.

This article is based on group discussions with physicians and public health nurses in child health stations of the Department of Health of New York City, and deals from a prophylactic point of view with the periods in which psychologic problems are most frequently encountered in infants and preschool children: namely, those of early feeding, weaning, thumb sucking, toilet training, anxieties and jealousy between siblings.

Feeding problems are traced to maternal attempts to get arbitrary amounts of the formula ingested, overrigid adherence to schedule, too hurried an introduction to the first solid food, impatience in urging food at the end of illnesses and unawareness of the need to allow for quantitative and qualitative variations in appetite, particularly during the second year. The desirability of satisfying the infant's sucking instinct is discussed, as well as the bearing this should have on when and how to wean and what to do for thumb sucking.

It is pointed out that there is a physiologic and psychologic readiness for intestinal and urinary control at various ages, and this should be considered in giving advice about training. The possessive attitude toward bowel function during the second year and the emotional tensions that interfere with retention of the urine are also considered.

It is also pointed out that children's emotional needs shift with age and that if these needs are not met anxieties result. The dependent 1 year old requires a constantly available mother, but at the same time needs freedom in order to develop his own independence. The 2 year old may react to abrupt parental absence with a state of anxiety. Many mothers do not understand their irreplaceability to very young children. If they must work, their children's security is more likely to be preserved by warm individual care than by that usually given in groups (day nurseries). Expert nursery school care can sometimes be substituted at the age of 2 to 3. On a part of a day basis it is constructive for most children. The 3 year old's imagination and capacity for identification often makes him apply remote and fantastic dangers to himself. Anxiety about his genitals is common and often leads to preoccupied masturbation.

Jealousy of a new baby may have various corrosive effects on the child's personality. Understanding efforts to minimize this sense of being displaced can be applied both before and after the baby's arrival.

The author in discussing each topic emphasizes the importance of anticipatory awareness on the part of physicians and parents, of where and when problems may arise and gives suggestions for routine advice to parents calculated to avoid

difficulties or to alleviate them promptly. These suggestions form the basis for summary statements on each topic indicating the way in which the information can be given parents.

AUTHOR'S ABSTRACT.

THE PSYCHOLOGY OF OBSTINACY. CHRISTINE OLDEN, Psychoanalyt. Quart. **12**:240, 1943.

Olden points out that stubbornness originally meant heroism and that psychologically obstinacy is a way of fighting to establish supremacy. In childhood it is a means of combating the threats imposed by the environment; later it is used to combat the threats of the super-ego.

Obstinacy is a protection against feelings of guilt and fear and is a means of combating anxiety, especially anxiety rooted in feelings of inferiority and humiliation. It enhances the feeling of omnipotence whenever self esteem is threatened by some real object or by the super-ego, since self esteem is unstable in obstinate people. Obstinacy is a function of the ego which develops during the anal period, for obstinacy is holding back for the purpose of opposing; but it also has an oral root in the baby's screaming when he wants to enforce his will.

Passive obstinacy is a compromise between aggressive feelings and anxiety. It is a good method of bolstering the self esteem but fails because it produces secondary guilt feelings and because it often conflicts with reality.

The analyst's attitude is important in analyzing obstinate patients. He should not meet obstinacy with counterobstinacy. He can help the patient by strengthening his ego through freeing him of his fears of the analyst. He can help by confronting the obstinate attitude with reality. He can increase the patient's self esteem by praising his efforts. PEARSON, Philadelphia. [ARCH. NEUROL. & PSYCHIAT.]

DEPRESSION—THE OEDIPUS CONFLICT IN THE DEVELOPMENT OF DEPRESSIVE MECHANISMS. EDITH JACOBSON, Psychoanalyt. Quart. **12**:541, 1943.

Jacobson reports the results of psychoanalysis in the case of a woman aged 24 who had a depression at 3½ years of age and again at puberty and finally one which brought her for psychoanalysis. Her father suffered from severe depressions. Jacobson places her condition in the manic-depressive group, but it was difficult to decide whether it might not be a severe anxiety hysteria with borderline depressions. Analysis showed that at the age of 3 there was the beginning of a normal oedipus situation. In the next half-year she suffered a series of traumatic incidents, among which was contact with her father's penis, which aroused her genital sensations intensely and prematurely and led her to expect a gratification from him similar to the gratification which she obtained from the frequent enemas given by her mother. She also had a frightening experience with a psychotic maid and recalled her mother's pregnancy with her brother. This series of traumatic incidents ended in a psychic collapse at the age of 3½ years. As a result of these incidents she felt disappointed by her father, and in bitter hate she turned away from him and back to her mother. Here, again, she was disappointed because the mother loved only the baby. In her disappointment and hostility she tried to escape into a narcissistic withdrawal and kill her need for love by becoming absolutely self sufficient and independent. In this goal she failed because of her intense ambivalence, as it was expressed in her fantasies of the primal scene—her wishes for participation in the sadistic fight of her parents and for their incorporation and annihilation. In vain she attempted to ward off her destructive impulses by identifying herself with the image of her good parents and by rebuilding her love relationship to them. The outcome of this conflict was her first depressive collapse. From that time she shifted her ambivalent desires from one parent to the other, without being able to establish a firm relationship with either. In her most balanced periods she found some security in her dependent but reliable bondage to her mother, competing with her brother by being the oversubmissive child. She invited her father's appreciation by her intellectual superiority.

This aggressive desertion of one parent for the other, with its guilty reactive sadomasochistic love, seems to be typical of the oedipus situation in cases of the manic-depressive psychosis.

After disappointment in the homosexual object the patient breaks away aggressively and approaches a heterosexual object. Unable to carry out this attachment because of ambivalence, he vainly attempts to return to the homosexual object. This attempt fails because of ambivalence. Then the patient goes into a depression.

PEARSON, Philadelphia. [ARCH. NEUROL. & PSYCHIAT.]

THE CAUSATION OF MONGOLISM AND ITS PROGNOSIS (ABRIDGED). MARCUS ENGLER, Proc. Roy. Soc. Med. **38**:211 (March) 1945.

The author divides the exogenous factors which have been postulated as influencing the pregnant uterus and thus contributing to the birth of an infant with mongolism, into three: (1) general exogenous factors, i. e. (*a*) exhaustion, (*b*) alcoholism and (*c*) syphilis; (2) increased amniotic pressure, and (3) the theory of nidation.

Each division is taken up separately and discussed. For such persons the prognosis as to life is bad, and the mental prognosis is certainly not good. Of 29 deaths of persons with mongolism who were under the author's supervision, 26 were from pulmonary complications. The purpose of the present paper was to show that many of the older theories have paved the way for the view that the unhealthy condition of the uterine mucosa, caused by various factors, is the only cause of mongolism.

WILLIAMSON, New Orleans.

MANAGEMENT OF THE DELINQUENT AND ABANDONED CHILD MUST BE THOROUGHLY TECHNICAL. PEDRO RUEDA, Arq. de pediat. **15**:7 (Dec.) 1943.

The author points out that in Argentina what is to be expected in accordance with the title of the article has not yet been reached.

Asylums and reformatories should be under the care of a specialized staff, without the interference of political factors.

LOZOYA, Mexico, D. F., Mexico.

EDUCATION OF CHILDREN AFTER AND OUTSIDE OF THE SCHOOL. MEGHIRA ESTELA, Bol. inst. internat. am. de protec. a la infancia **18**:401, 1944.

The author concludes that one of the better things to improve the education of children is reading during the leisure hours (six to seven hours daily). In order to obtain good results, more libraries and cheaper books and texts should be provided.

LOZOYA, México, D. F., Mexico.

Diseases of the Ductless Glands; Endocrinology

STATUS THYMICO-LYMPHATICUS. JESSE L. CARR, J. Pediat. **27**:1 (July) 1945.

In reviewing 521 cases of sudden death of persons under the age of 12 years recorded in the San Francisco City and County Coroner's Office, all cases in which death could be ascribed to causes other than those associated with a thymus lymphatism, changes in the cortical regions of the adrenal glands or lymphatic infiltration around the bronchioles were discarded. This left 43 deaths distributed into three categories: 1, acute asphyxia from tracheal compression and distortion of the intrathoracic contents by a greatly enlarged thymus gland; 2, thymic hyperplasia and hypertrophy, with adrenal atrophy and insufficiency; 3, an asthmatic status which is characterized by a definite peribronchial lymphocytic infiltration, bronchial musculature of the hypertrophic type, mucous plugs within the bronchial channels and also a diffuse lymphatism of greater or lesser degree associated with changes of the thymus, usually hyperplastic in nature.

The term status thymicoasthmaticus is proposed as applying a proper anatomic and clinical term to sudden death associated with this type of anatomic and

pathologic change which is believed to be congenital. These changes have been observed in babies taken in utero, as well as in those recently born and those who have lived several months.

Also tabulated and commented on were cases of sudden and dramatic involution of the thymic tissue, both cortical and medullary, in the presence of cachexia, inanition, starvation, electric shock and wasting diseases.

Sudden death in children resolves itself as a problem into many components. There is of course no one cause, and in our series of well over 500 autopsies on children dying suddenly, the problem of thymus enlargement is a secondary one. Strangely, however, enlargement of the thymus gland, lymphatism, hypoadrenalism and similar related conditions have been displaced even from secondary positions of importance as causes of disease and death and have been thrown into disrepute by articles in the medical literature which are based more on precedent and fashion than on observation.

The now popular attitude that there is no such thing as status thymicolymphaticus can be quickly dissipated by studies at autopsy in any coroner's office where children are studied, and the widespread belief that an enlarged thymus in itself will not cause asphyxia by tracheal compression and distortion can be disproved at necropsy wherever studies are done on cases of sudden death in children.

On the other hand, when once accepted, status thymicolymphaticus and related terms become far too easy to use. Instead of being reserved for specific cases to which they are properly applied, such diagnoses are generically used to explain many sudden deaths in children for which there is no other obvious cause. It may be that such diagnostic abuses have in the main been responsible for the disrepute of the thymic status.

We now feel that orderly proceedings at necropsy will segregate the various causes of asphyxia in infants, asphyxia being by far the commonest cause of sudden death under the age of 2 years, and that such studies will in their natural evolution reestablish the relationship of enlarged thymus glands, lymphatism, adrenal hypoplasia and such conditions, either isolated or related, as veritable, tenable, direct and sole causes of death.

AUTHOR'S ABSTRACT.

BONE GROWTH IN CONGENITAL MYXEDEMA. PAUL V. WOOLLEY JR. and ROBERT W. MCCAMMON, J. Pediat. **27**:229 (Sept.) 1945.

The authors reach the following conclusions: Characteristic changes in the long bones of cretins are of diagnostic value and also serve as guides to the regulation of treatment.

A curve expressing the growth of the radius in infants without evidence of thyroid deficiency is presented.

Several cases are reviewed to illustrate the use of studies of the long bones.

AUTHORS' CONCLUSIONS.

THYROID GLAND IN CHILDHOOD. OCTAVIO LEMBRUGER, Arq. de pediat. **16**:7 (June) 1944.

After stressing the importance of the thyroid gland in organic development, its influence on infectious diseases and mental and intellectual development, a division of diseases affecting the gland is made in three groups in accordance with the etiologic factors: (*a*) diseases with alterations of the endocrine functions, (*b*) diseases with decreased endocrine functions and (*c*) diseases with increased endocrine functions.

All of these groups are quite rare during childhood, appearing only as slight or incomplete forms of infantile myxedema, Brissaud's myxedemic infantilism, hypothyroid or hyperthyroid temperament, or mongolism.

Each one of these forms is described, especially congenital myxedema, from the birth of the infant to the age of 3 years, considered from a general and a roentgenologic point of view.

The latter is very important owing to the influence of the gland over the bony development. The report ends with a review of the diagnosis, prognosis and treatment and a consideration of some of the case reports.

LOZOYA, México, D. F., Mexico.

A CASE OF PUBERTAS PRECOX IN MONGOLOID IDIOT. M. SCHACHTER and S. COTTE, Ann. pædiat. **160**:104 (Jan.-Feb.) 1943.

A case of pubertas precox in an 11 year old mongoloid idiot is reported. Brain pressure and endocrine tumors are excluded. Only 1 such case has been published during the past twenty years. As to pathogenesis, disturbance of brain development is considered whereby in addition to changes in cortical structure, softening in the region of the tuber cinereum is also suggested.

AUTHORS' ABSTRACT.

A CASE OF SYMPATHICOBLASTOMA IN AN INFANT AGED ONE MONTH. TAGE ESPERSON, Ugesk. f. læger **106**:1141, 1944.

The case of a 5 week old girl with sympathicoblastoma of the adrenal gland and pronounced metastasis of the liver is reported. The weight of the liver corresponded to that of a child of 12.

WALLGREN, Stockholm, Sweden.

Diseases of the Muscles, Bones, Joints and Lymph Glands

A CASE OF HURLER'S DISEASE (LIPOCHONDRODYSTROPHY). H. R. SEAR and J. K. MADDOX, M. J. Australia **1**:488 (May 12) 1945.

The authors describe the clinical and roentgenographic aspects of an extreme case of lipochondrodystrophy (gargoylism) in a girl aged 2 years. The chief clinical features were scaphocephaly, with an overhanging forehead, grotesque facies, bilateral corneal opacities, hepatosplenomegaly, lumbar kyphosis, short arms and mental retardation. The roentgen studies showed advanced osseous age, expansion of the long bones, deformity of lower ends of the radiuses and ulnas, wedging of the bases of metacarpals, alteration in trabeculation of bone, enlargement of the sella turcica and delay in closure of the anterior fontanel. Consanguinity of the parents was present but is not considered a factor.

GONCE, Madison, Wis.

PSEUDOLUXATIO COXAE CONGENITA. ROBERT LENK and ERICH NASSAU, Ann. pædiat. **162**:307 (June) 1944.

1. In a fairly large number of cases showing the same clinical symptoms as congenital luxation of the hip joint only signs of a disturbance of ossification in the nucleus of the head of the femur are observable roentgenologically. This condition, for which we suggest the name pseudoluxation of the hip, heals completely without any treatment whatever. It is apparently more common than the real luxation. It is probable that a part of the early diagnosed and successfully treated luxations of the hip belong here.

2. Since in the orthopedic treatment of such conditions the danger of secondary necrosis of the femoral head is not negligible, the necessity arises for a revision of the indication for early treatment. Suggestions, therefore, are given.

3. The genesis of the anomaly has so far not been cleared up. A number of possibilities are discussed in the report, and attention is drawn especially to certain similarities in our observations to those of many endocrine insufficiencies, as also to the possibility of genetic relations of pseudoluxation to genuine congenital luxation.

AUTHORS' ABSTRACT.

CALCIUM AND PHOSPHORUS METABOLISM IN OSTEOMALACIA. KUNLY WANG, S. H. LIU, H. I. CHU, T. F. YU, H. C. CHAO and H. C. HAU, Chinese M. J. **62**:1 (Jan.-March) 1944.

The writers state that the body absorbs rather poorly the calcium and magnesium of phytin and the calcium and magnesium salt of phytic acid, which is widely distributed in foodstuffs and is noteworthy in cereals, in which it makes up 50 to 70 per cent of the total phosphorus.

An experimental study of 2 patients who had moderately severe osteomalacia is reported. The experiments are given in detail for the purpose of determining the availability of phytin phosphorus, either from cereals or from phytin preparations. The conclusion is reached that the absorption and retention of calcium and phosphorus were lower when phytin was the source than when a similar level of inorganic phosphorus was provided in the intake. This is explained on the basis of the impaired utilization because of limited hydrolysis and incomplete absorption of the hydrolyzed phytin. Vitamin D, known to be capable of promoting the absorption and retention of calcium and total phosphorus did not show a clearcut enhancing effect on the utilization of phytin. An important contributing factor to the pathogenesis of osteomalacia is a diet high in cereal or phytin.

LOZOYA, México D. F., Mexico.

MULTIPLE CHRONIC INFECTIOUS ARTHRITIS IN CHILDHOOD (ATYPICAL CASE OF MORBUS STILL). FRITZ HARVING, Nord. med. (Hospitalstid.) **24**:1821 (Oct. 13) 1944.

The author reports a case of chronic arthritis in a girl aged 10. The characteristic feature of the case was the dominant infectious element, while the arthritic symptoms were less pronounced. The author concludes: There seem to be three variants of chronic multiple infectious arthritis in childhood: the type described by Still, the type described by Monrad (afebrile with pronounced arthritis) and the reported type with septic fever and slight arthritic symptoms.

WALLGREN, Stockholm, Sweden.

Skin Diseases; Allergy

GASTRIC SECRETION IN INFANTILE ECZEMA. ALBERT STRICKLER, ALBERT HERMAN and HELEN GRUMACH-FABIAN, Arch. Dermat. & Syph. **51**:189 (March) 1945.

Fifty children who had infantile eczema were subjected to a gastric analysis. The hydrochloric acid secreted in the stomach of each child was found to be normal in amount.

MCINTOSH, Iowa City, Iowa.

NUTRITIONAL SURVEY OF THREE HUNDRED AND FIFTY-FOUR DERMATOLOGIC PATIENTS. J. LAMAR CALLAWAY, D. F. MILAN and RAY O. NOOJIN, Arch. Dermat. & Syph. **51**:266 (April) 1945.

A nutritional survey of 354 patients who had various dermatologic diseases was made at Durham, N. C. The dietary histories and the blood studies (vitamin A, ascorbic acid, carotene and hemoglobin) of these patients were not found to differ significantly from those of the general population of the area. The authors concluded that the nutritional status was not a factor in precipitating the dermatologic diseases of the patients studied.

MCINTOSH, Iowa City, Iowa.

SOME PHASES OF VITAMIN THERAPY IN DERMATOLOGY. MAXIMILIAN E. OBERMAYER and KENDAL FROST, Arch. Dermat. & Syph. **51**:309 (May) 1945.

A review of the use of vitamins in the treatment of skin diseases is presented. The authors recommend the use of the vitamins of the B complex for the manage-

ment of dermatosis in which allergic factors are involved. Vitamin A preparations are reported as being beneficial in the treatment of diseases characterized by excessive or abnormal keratinization. Large doses of the vitamins are recommended for the treatment of these conditions.

McINTOSH, Iowa City, Iowa.

ETIOLOGY OF KAPOSI'S VARICELLIFORM ERUPTION. RUSSELL J. BLATTNER, FLORENCE M. HEYS and MARY LOU K. HARRISON, J. Pediat. **27**:207 (Sept.) 1945.

Kaposi's varicelliform eruption is a comparatively rare exanthem occurring in patients with atopic eczema. The illness is characterized by a high fever for from four to seven days, by leukopenia and by the presence of umbilicated vesicles, some of which may become pustular. Only the eczematous portions of the skin are involved. The disease is self limited, and in general the prognosis is good.

A filtrable virus (Berkefeld V-13 "fine" and N filters) isolated from the cutaneous lesions of a 15 month old child with a clinical picture typical of Kaposi's varicelliform eruption was identified as a member of the herpes group. It is noteworthy that the virus was isolated not only by means of the rabbit's cornea but also directly on the chorioallantois of the developing hen's egg. The latter observation would seem to exclude any possibility that a latent herpes virus might have been reinactivated in the rabbit by experimental manipulation.

It seems logical to conclude that a strain of herpes virus is the etiologic agent involved in at least some of the cases diagnosed as instances of Kaposi's varicelliform eruption.

AUTHORS' ABSTRACT.

NASAL ALLERGY IN CHILDHOOD. H. A. E. VAN DISHOECK, Maandschr. v. kindergeneesk. **10**:232 (March) 1941.

Among 500 children with diseases of the ear, nose and throat from 3 to 15 years old, 65 patients suspected of allergy were selected by means of interrogation and examination. Among them 50, namely, 10 per cent of the total, showed positive cutaneous reactions, chiefly for inhalants but in some cases also for food allergens. Sensitivity to more than one allergen was present in 41 patients; only 3 patients with hay fever uncomplicated by other conditions were found. In 35 cases asthmatic complaints were noted. Eosinophilia of the blood and increase of the mononuclear cells were present in almost every case. Other evidences, such as eosinophilic cells in the nasal secretion, allergic edema of the antrums, allergic degeneration of the turbinates, a history of eczema in the past and a contributory family history, were each present in 50 per cent of the cases. No coincidence of any kind was found between the symptoms of the allergic disease. Many patients could be cured by means of elimination of the offensive allergens. Desensitization to house dust was successful. Perhaps the tracing and the treatment of nasal allergy in children will be of great importance in the prevention of asthma in adults.

VAN CREVELD, Amsterdam, The Netherlands.

Teeth and Dentistry

THE RELATION BETWEEN FOOD AND CONDITION OF THE TEETH. B. C. P. JANSEN, Maandschr. v. kindergeneesk. **10**:295 (April) 1941.

Recent researches on food and metabolism have shown in animal experiments that a deficiency of ascorbic acid or of vitamin D, an excess of fluorine in the food and other factors give rise to all kinds of deviations of the normal construction of the teeth and in this way also to deviations of the normal resistance of the teeth. Numerous observations in men can also only be explained by assuming that the alarming frequency of caries in the civilized peoples is caused by food which in this respect is not optimal. However, much research work still must be done in order to give exact indication of which way the Dutch food should be modified or completed so that it will be the most favorable with respect to the condition of the teeth.

VAN CREVELD, Amsterdam, The Netherlands.

News and Comment

GENERAL NEWS

The Scientific Exhibit, Atlantic City Session of the American Medical Association.—At the Atlantic City Session, June 9 to 13, 1947, the American Medical Association will observe its centennial anniversary. For almost half of those hundred years—since 1899—the Scientific Exhibit has been a feature of each annual session and has developed into a short course in graduate medical instruction.

Exhibits at the 1947 Session will cover all phases of medicine. A certain amount of historical material will be included, but emphasis will be placed on the latest developments of medical science. The representative to the Scientific Exhibit from the Section on Pediatrics is Dr. Albert V. Stoesser, 412 Delaware Street S. E., Minneapolis.

Applications for space should be submitted as early as possible, since the closing date is Jan. 13, 1947. Application blanks may be obtained either from Dr. Stoesser or from the Director, Scientific Exhibit, American Medical Association, 535 North Dearborn Street, Chicago 10.

International Hematology and Rh Conference.—The international Hematology and Rh Conference will be held in Dallas, Texas, on Nov. 15, 1946, in affiliation with the Second Mexican Blood Transfusion Congress, which meets in México, D. F., Mexico, Nov. 17-25, 1946.

The morning session will be held at the Adolphus Hotel. Dr. Joseph M. Hill, Director of the William Buchanan Blood, Plasma and Serum Center, Baylor University Hospital, will preside. The afternoon session will be held at the Medical Library of Baylor University Hospital. Dr. Eduardo Uribe Guerola, President of the Second Mexican Blood Transfusion Congress, will preside. The guest speakers are: Dr. Philip Levine, Ortho Research Foundation, Linden, N. J.; Dr. R. R. Race, Lister Institute of Preventive Medicine, London, England; Dr. William Dameshek, Tufts College Medical School, Boston; Dr. Ernest Witebsky, University of Buffalo School of Medicine, Buffalo; Dr. I. Davidsohn, University of Illinois College of Medicine and Mount Sinai Hospital, Chicago; Dr. Louis K. Diamond, Harvard Medical School, Boston; Dr. Ludwig Hirszfeld, University of Wroclaw, Wroclaw, Poland; Dr. Ignacio Gonzalez Guzman, University of Mexico College of Medicine, México, D. F., Mexico; Dr. E. Uribe Guerola, University of Mexico College of Medicine, México, D. F., Mexico, and Dr. J. M. Hill, Southwestern Medical College and Baylor University Hospital, Dallas, Tex.

Arrangements for housing accommodations may be made by notifying Dr. Sol Haberman, William Buchanan Blood, Plasma and Serum Center, Baylor University Hospital, Dallas, Tex., before Nov. 5, 1946, to insure reservations for rooms.

Society Transactions

AMERICAN PEDIATRIC SOCIETY

Harold K. Faber, M.D., *President*

Henry G. Poncher, M.D., *Secretary-Treasurer*

Fifty-Sixth Annual Meeting, Skytop, Pa., May 1-3, 1946

Services of Dextrose in Parenteral Fluid Therapy. Dr. Allan M. Butler, Dr. James L. Gamble, Dr. Nathan B. Talbot, Dr. E. A. MacLachlan and Dr. J. Appleton, Boston.

The data presented were taken from a study of the problem of provisioning castaways. With adult volunteer subjects, the outgo of nitrogen, of sodium and of organic acids in the urine were measured over six day periods of fasting and over subsequent periods in which dextrose was given orally at several levels of intake. It was found that maximal sparing of protein is gained by an intake of 100 Gm. of dextrose daily and amounts to reduction of consumption of body protein to about one-half the extent found during fasting. It was also found that loss of sodium is reduced to the same extent and that this effect is produced by an intake of 50 Gm. of dextrose daily. The ketosis of fasting was dependably prevented by 50 Gm. of dextrose. From measurement of the total output of solute in the urine, the renal water requirement for a person subsisting on 100 Gm. of dextrose was found to be 700 cc. daily. Taking into account the other components of the water exchange, the water intake requirement was estimated as 1,200 cc. These results define the requirement for water and dextrose in parenteral fluid therapy as 1,200 cc. and 100 Gm. daily in situations in which it is not necessary to attempt to provide a full calory intake parenterally.

DISCUSSION

Dr. Daniel C. Darrow, New Haven, Conn.: In reducing the intake and the outgo of the adult to that of a baby and expressing the results per kilogram, did you take account of the caloric difference? Did you reduce the water intake to a per kilogram basis or a per calory basis?

Dr. J. L. Gamble, Boston: I have always assumed that as a rough approximation the water requirement of the infant per kilogram is twice that of the adult because his energy expenditure is twice as large. Of course, what we really want is data obtained directly from children and infants in relation to age.

Dr. Harold E. Harrison, Baltimore: What was the effect of giving dextrose on the p_H of the urine? Is it possible that the sodium-sparing effect of dextrose could be a renal effect?

We think that perhaps changes in the p_H of the urine as finally elaborated may influence renal tubular function with regard to other ions. Could it possibly do so with respect to sodium?

Dr. J. L. Gamble, Boston: One would expect to find the p_H lower in fasting than when dextrose is given. Actually, however, there was no appreciable change in p_H. The value in both periods was in the neighborhood of p_H 6.0. This would seem to indicate that the extension of titratable acidity found during fasting was composed entirely of the fraction of the ketone acid excretion which is "free" at this p_H.

Dr. Harold E. Harrison, Baltimore: Is it possible that changing of the p_H makes the renal tubular reabsorption of sodium more efficient?

DR. J. L. GAMBLE, Boston: That I do not know.

DR. IRVINE MCQUARRIE, Minneapolis: Dr. Gamble, what do you think is the mechanism of this sparing effect on the water caused by the giving of dextrose? I hit right away at the idea of preventing the ketosis. You have ruled that out.

DR. J. L. GAMBLE, Boston: An offhand explanation would be that ketosis leads to loss of sodium. We find, however, that the increase in acid excretion caused by ketosis is closely covered by extension of titratable acidity of the urine together with an increased production of ammonium. So there is no evidence of relation of the larger loss of sodium during fasting to ketosis. We have, then, no explanation to offer for the sodium-sparing effect of dextrose.

DR. L. EMMETT HOLT JR., New York: I should like to ask if Dr. Gamble and Dr. Butler have data indicating that this water-sparing, sodium-sparing action lasts more than the first days of an experiment.

DR. J. L. GAMBLE, Boston: Over the first few days of fasting the loss of sodium was relatively much larger than the loss of potassium. By the end of the six day period, the losses were roughly proportionate to the relative quantities of sodium and potassium in the body. This was also found when dextrose was given, the absolute losses being, however, about one half as large as during fasting.

DR. GEORGE M. GUEST, Cincinnati: I should like to ask Dr. Gamble if the protein and electrolyte-sparing effects of dextrose in circumstances such as he describes may be regarded as in accord with analogous observations made in studies of diabetic acidosis. During the development of ketosis and acidosis in the diabetic person there is a great expenditure of sodium, potassium and phosphates, which has been thought to result largely from the breakdown of organic phosphates in the tissue cells of the body. During recovery, sodium and potassium are restored to the cells concomitantly with resynthesis of organic phosphates. Dextrose is a necessary substrate for the processes of phosphorylation by which these compounds are restored to the cells as well as for the maintenance of the compounds at normal concentrations. The chemical reactions involved may be most easily traced in the red cell, regarded as the prototype of other cells of the body so far as these reactions are concerned. The fact that dextrose is essential to these processes for maintenance of cellular constituents (or for their restoration after depletion, as the case may be) may be cited as an argument in favor of the administration of dextrose early in the treatment of acidosis and dehydration. Inasmuch as it has been calculated that the dextrose circulating in the blood can supply only enough calories for ten to fifteen minutes of normal energy expenditure, it is obvious that tissue stores are drawn on continuously for the normal metabolism of the body. Presumably the administration of extra dextrose exerts the sparing effect by diminishing the drain on the tissue stores and the catabolism of many interrelated constituents of the cells.

DR. J. L. GAMBLE, Boston: I can only say that I would guess that the explanation of this sodium-sparing effect of dextrose will be found by following the path which Dr. Guest has suggested.

Retentions of Electrolyte During Recovery from the Dehydration of Severe Diarrhea. DR. DANIEL C. DARROW, New Haven, Conn.

Balances of nitrogen and the chief electrolyte were determined for 6 babies during recovery from the severe dehydration of diarrhea. From the balances and serum concentrations the probable distributions of the electrolyte were calculated by assuming that the electrolyte retained indicated the probable deficits during dehydration, an insight into the changes in the body during diarrheal dehydration was obtained.

Deficit of potassium in excess of that accounted for by loss of nitrogen was a regular feature of the cases of diarrhea. In certain patients sufficient sodium was transferred from extracellular to intracellular fluids to explain the greater part of the deficit of extracellular sodium and the reduction in serum bicarbonate con-

centration. In other patients deficit of intracellular as well as of extracellular sodium developed. Changes in intracellular phosphorus were not large.

Treatment with solutions containing only sodium and chloride led to the transfer of large amounts of sodium to the intracellular fluids and was frequently accompanied with low concentrations of potassium in the serum. Treatment with potassium chloride as well as with sodium chloride and sodium lactate led to the retention of larger amounts of potassium not accompanied with retention of nitrogen. In these circumstances increases in intracellular sodium were minimal. The deficit of potassium was equal to about one fourth of the calculated potassium of the body in the most severe diarrheas.

A clinical trial of a form of treatment based on these findings was made with the assistance of Dr. Clifton Govan. Such a treatment reduced the mortality to about 4 per cent. In a similar number of apparently similar cases there was a mortality of 25 per cent when the patients were treated in the usual manner.

DISCUSSION

DR. SAMUEL RAPOPORT (by invitation), Cincinnati: We have also been interested in the losses of intracellular ion at Children's Hospital Research Foundation but have not been in a position to make so extensive a study as Dr. Darrow. From the report in the paper that Dr. Harrison read this morning and from some of the data that Dr. Darrow just presented, it would seem that one is dealing with changes concerning not potassium alone, but also phosphorus and calcium. These three ions may be classified as nonextracellular. Potassium is primarily intracellular; calcium belongs mostly to the supporting structures of the body, and phosphorus occurs in both the soft tissues and the bone.

[Slide] The data on a premature infant 1 month of age who weighed a little over 2 Kg. are presented. The child had diarrhea, which was proved to be due to a virus, and that is an exceedingly protracted, recurrent form of diarrhea. The main point made is that during the period from the eleventh to the sixteenth day of the illness, at a time when the diarrhea had stopped and the values of p_H and carbon dioxide were normal, there were found low concentrations of calcium, potassium, phosphorus and phosphatase in the plasma.

During the postacidotic period after the stopping of the diarrhea, the infant experienced several untoward reactions. It repeatedly stopped breathing, and once had a period of convulsions. Similar observations of untoward reactions following recovery from acidosis were made in other cases. Even before we studied such cases, we had been familiar with the experience that after the period of acidosis convulsions occurred and sometimes a so-called "false recovery"; that is, an infant that seemed well hydrated suddenly collapsed, began to breathe badly, and was drowsy and at the same time irritable.

For an understanding of the course of diarrhea we adopted the concept of two phases of the illness: the period of acidosis, during which losses occur of intracellular and extracellular fluid with its ions and also losses from the bony structures, and a subsequent period following the acidosis, during which the body cells recuperate from their losses and quickly recapture fluid and ion. During the period of intracellular recovery the concentrations of potassium, phosphorus and calcium in the extracellular fluid tend to be low. The level of these ions in the plasma indicates the direction and perhaps the intensity of the process of recovery.

The reduction of the phosphatase activity in the plasma we have tentatively explained on the assumption that less phosphatase may escape from bone during a period of active deposition of calcium and phosphorus.

[Slide] Three patients were given sodium lactate with the formula. They were overtreated in the postacidotic period. We have found alkalosis more liable to develop in such patients. It may be seen that in each case the bicarbonate and the p_H of the plasma rose to high values and that the potassium, calcium, phosphorus and phosphatase dropped to low levels. The patients were edematous at that time. In each case after correction by giving calcium chloride a return to normal in all constituents of the plasma ensued and the edema subsided.

[Slide] Four patients are presented who received therapy with bicarbonate for correction of the acidosis of diarrhea. These were all extraordinarily severe diarrheas of the type Cincinnati is so familiar with. Values of bicarbonate, calcium, phosphorus and phosphatase at the time of the patient's admission and after administration of bicarbonate are listed. After correction in each case there was a lowering of calcium as well as of phosphorus and phosphatase. In the last patient reported on convulsions developed and also a series of other complications which time does not permit me to describe.

In summary, there is perhaps a triad of change concerning the potassium, calcium and phosphorus ions. Which of the three ions is the most important to correct, I am not certain. Perhaps the wisest thing is to correct all 3. There are certain practical difficulties. One cannot very well give calcium and phosphorus intravenously at the same time. One can do that well with calcium and potassium.

We have been impressed by the dangers of hypocalcemia. In our experience the postacidotic phase of diarrhea is dominated by the low calcium in the plasma. In addition to the typical features of tetany that have been earlier associated with that disease, other manifestations have been found: strabismus and nystagmus; a deviation of the balance of the autonomous nervous system, which expresses itself in changes of the rate and character of breathing, of intestinal motility and of the tone of capillaries; and finally hemorrhagic manifestations which from predilection occur in the central nervous system and in the intestinal tract.

DR. ALLAN M. BUTLER, Boston: I should like to ask, first, what the serum proteins were and, second, what the clotting time was for the newborn babies.

DR. SAMUEL RAPOPORT, Cincinnati: We had determined the serum protein values continuously for many of these babies. It is quite true that the protein is low. It is often low on admission and hardly changes later. The calcium returns to normal while the serum protein may still be low. We have been much interested in prothrombin time. In 7 cases of protracted diarrhea, extraordinary prolongations of prothrombin time have been noted. The hemorrhagic tendency that we observed so often with hypocalcemia was not associated with hypoprothrombinemia.

DR. IRVINE MCQUARRIE, Minneapolis: I should like to ask if Dr. Darrow has done any postmortem studies of tissue electrolyte on babies that have not been given a large amount of potassium. I should like to know how much that contributes to the death of these patients.

DR. DANIEL C. DARROW, New Haven, Conn.: I observed lowering of serum calcium once or twice several years ago. Nothing was done about it, but I am sure that decrease in serum calcium is an important phenomenon. If one reads the early papers of Drs. Schloss and Stetson and of Drs. Marriott and Holland, who first demonstrated the lowering of the serum bicarbonate in diarrhea and showed that this could be restored by giving sodium bicarbonate, it will be found that both papers state that restoration of the serum bicarbonate by giving bicarbonate seemed to produce an immediate improvement in the children that was not fulfilled by a subsequent drop in the mortality.

At present we are not in a position to state the reasons for the disappointing results. I think we shall have to have more studies in which we actually observe the concentration of serum calcium in conjunction with balance studies. We determined the concentration of serum calcium only in the first case, in which the disease was the mildest; perhaps this determination should not be used as evidence that a low concentration of serum calcium is not of frequent occurrence. There is the possibility that administration of potassium prevents liberation of phosphorus from the cells. A high concentration of serum phosphate might tend to lower the serum calcium, and hence the new treatment may obviate this difficulty observed by Dr. Dodd. Obviously, overtreatment with sodium bicarbonate would aggravate the tendency to tetany.

The other adverse effect that the administration of sodium bicarbonate might produce is the increase in intracellular sodium. When Hartmann calculated the dose of sodium bicarbonate necessary to restore the serum carbon dioxide in

acidosis, he multiplied the deficit in the concentration of serum bicarbonate by the volume of total body water. It is obvious, according to the literature, that sodium is chiefly an extracellular ion. However, if sodium enters the extracellular fluids in order to replace the deficit of bicarbonate, and if it should also enter the intracellular fluids in order to replace the deficit of potassium which we demonstrated in these cases, the dose of bicarbonate that would be necessary to treat acidosis would be enormous, and the intracellular fluids would acquire an extremely high content of sodium and at the same time would not overcome the deficit of potassium.

We do not know exactly how harmful a high sodium and a low potassium content in the cells are. We know that if one gives an animal a diet low in potassium this distorted pattern of muscle electrolyte can be produced and is accompanied with definite necrosis of the heart, and that the same picture can be produced by repeated injections of desoxycorticosterone acetate.

I think you are all familiar, from the descriptions of dehydration in diarrhea, with the fact that slowing of the heart is one of the most ominous signs that develops in diarrhea. While anatomic lesions have not been described, I do not think one can be sure that there are not functional disturbances in the heart that accompany the deficits of potassium.

We have analyzed 5 or 6 muscles of babies dying with diarrhea. Two or 3 of them had received no treatment, and the others had received the older form of treatment. The deficit of potassium that we found in the muscles was about 40 per cent of the normal content. That is sufficient to account for the deficits which we described as present in the babies of the metabolic study.

While I should not leave the impression that the deficits of potassium do not involve other tissues than the muscle, I am sure that the muscles are the chief tissues that account for the deficit of potassium.

One other thing that I think must be kept in mind is that it is probably too simple to assume that the excretion of potassium in the stools is the sole explanation of these changes. In the first place, Fox has analyzed muscle subjected to tourniquet shock, and the analyses show a tendency for the muscles to lose potassium and to have sodium enter the cells. The circulation of the babies with pronounced dehydration gives all the clinical picture of shock. Hence part of the loss of potassium observed is probably accounted for by the syndrome of shock that develops.

For these reasons I think the initial disturbance is accounted for by the diarrhea and the loss of potassium in the stools, but, in addition, the tissues probably cannot retain potassium or tend to lose it if they are in the condition of shock. Hence I would not recommend that one should institute the treatment of diarrhea without first going through the ordinary measures which we take to overcome circulatory changes; that is, I think these children all need initially the intravenous injection of saline and dextrose solutions and the transfusions, and then, when their circulation is somewhat improved, they should be given parenteral injections of a solution containing potassium.

I should also like to point out that these enterprising physicians in Baltimore have found it is simple to carry out this treatment, because after treating the patients for the initial deficit by intravenous means which takes twelve to twenty-four hours, the solutions containing potassium can be given by mouth, provided no milk is added to them.

Effectiveness of Alkali Therapy in the Treatment of Experimentally Induced Acidosis. Dr. Waldo E. Nelson, Dr. Esther M. Greisheimer, Dr. M. J. Oppenheimer and Dr. Howard W. Robinson, Philadelphia.

In view of existing differences of opinion, an attempt has been made to secure more specific information concerning the efficacy of parenterally administered alkali in the treatment of acidosis of severe degree. The problem at issue may be stated as follows: Is there a period in the clinical course of severe states of

acidosis of whatever cause when the administration of an appropriate amount of alkali might prevent otherwise irreversible damage?

Dogs whose plasma p_H and carbon dioxide content were within the normal ranges were made acidotic by administration through a gastric tube of a 4 per cent solution of ammonium chloride at intervals of two hours from 10 a. m. to 4 p. m. The administration of this acid salt was continued until the p_H level on the following morning was extremely low (values below 7.10, mostly below 7) and until the dog appeared to be in an extremely critical condition. The clinical manifestations consisted of ataxia, anesthesia, collapse, vomiting and hemorrhagic diarrhea.

At such a point, the dog was either treated with sodium bicarbonate (the dose calculated from experimental observations of Palmer and Van Slyke and administered in a 5 per cent solution) or he was assigned to the control group. In order to subject therapy with alkali to a rigid test and to avoid as many variables as possible, no other parenteral fluids were administered and the dogs were allowed to eat and drink as they desired.

Forty dogs were made severely acidotic; of these, 18 were treated with sodium bicarbonate, and 22 served as the control group. Twelve, or two thirds, of the treated group recovered in contrast to recovery of only 7, or one third, of the control group.

When the groups were subdivided on the basis of the length of time that the individual dogs were in a state of acidosis with a plasma p_H below 7.10, it was found that the duration of acidosis of such an extreme degree was a significant factor in relation to recovery. Twenty-two dogs had a plasma p_H level below 7.10 for a period longer than twenty-four hours. Of these, 12 were treated with bicarbonate, and 10 were in the control group. Six, or one half, of the treated group recovered in contrast to only 2, or one fifth, of the control group. Of the 18 dogs whose plasma p_H was below 7.10 for less than twenty-four hours, 6 received bicarbonate and 12 were in the control group. All of the treated dogs recovered in contrast to only 5, or approximately one half, of the control group.

While it is still impossible to state an exact critical level of the plasma p_H or an exact critical period of acidosis at a given level of p_H, it seems apparent that there is a critical phase which must be based both on depth of p_H and duration of acidosis at a given level. The latter, within the limits of this study, would appear to be more important. When the p_H varies from 6.9 to 7.10, the critical period would appear to be in the range of twenty-four to forty-eight hours. The administration of appropriate amounts of alkali prior to this time increases the chances of recovery.

DISCUSSION

DR. ALEXIS F. HARTMANN, St. Louis: I have been much interested in all three papers this afternoon, and I am glad that I am not in the position of that wit who once said that he had heard a lot, but everything that was true he knew beforehand, and everything which was new, unfortunately, was not true. I have learned much, but I should like to emphasize a few things that you know but perhaps need to have your memories refreshed on a little. One concerns the use of alkali in the different types of acidosis.

Much the same studies that Dr. Nelson made experimentally I have made clinically as subjects were treated for acidosis. For instance, I have much the same sort of data on diabetic persons that Dr. Nelson has presented, but there is one feature every one could profit by remembering: Hyperpnea is a poor clinical index of the severity of acidosis and acidemia. In Gamble's studies, he has mentioned frequently that the respiratory defense was about 50 per cent efficient. Now that is the average figure, but in many subjects the efficiency is a great deal less. That seems to be true in extremely young babies, and particularly in premature babies and in diabetic children in whom acidosis has gradually developed and continued severe for a number of days.

My experience has been that in that group one would expect to find the lowest p_H's of the blood, and in every instance of a bicarbonate of less than 10 volumes

per carbon dioxide content, a p_H less than 7. Such children should have been breathing better; and if one takes movies of their recovery one will find something most interesting. As they improve in circulation and strength, hyperpnea increases. In two or three hours after improvement has definitely set in, the hyperpnea is sometimes frightening, but when the acid-base balances of their blood are plotted on Hastings' charts—and such measurements have been made every fifteen minutes during recovery—one sees what is really happening. Recovery is marked almost entirely by recovery of p_H during the first two hours. A p_H of 6.8 in one instance went up to 7.2, whereas bicarbonate rose only from 4.2 to 6 mm. per liter. I think the failure of some persons to recognize this fact led to an erroneous conclusion that both sodium lactate and sodium bicarbonate sometimes fail to relieve acidosis. One may give the recommended dosage, 60 cc. per kilogram of body weight of one sixth molar solution, and yet the bicarbonate content of the blood may go up only 10 or 15 volumes per hundred cubic centimeters when an increase of 40, 50 or 60 volumes per hundred cubic centimeters is indicated.

I am sure that this must be due to the claiming of sodium release from lactate or bicarbonate by acids stronger than carbonic. When the p_H of the plasma is below 7, the isoelectric point, practically, of hemoglobin and the other proteins has been reached. When the p_H rises from 6.8 to 7.2 or 7.3 or 7.4, they become stronger acids again, and claim more base, and the sodium released from lactate really is dissipated in satisfying such buffers and cannot appear as sodium bicarbonate.

DR. ALLAN M. BUTLER, Boston: I should like to make one point—which is more pertinent today than it was yesterday now that physicians are beginning to learn something about this entrance of sodium into cells in which sodium does not belong. It concerns this habit of calculating the requirement of sodium in the correction of acidosis.

Dr. Darrow has pointed out one limitation in the accuracy of the calculation when made on the basis of total body water having the normal bicarbonate content of serum, a calculation which results in a figure that may be almost 100 per cent too great.

The other method sometimes used is derived from a paper by, I think, Palmer and Van Slyke in 1916, in which they measured how much sodium bicarbonate had to be given to 12 patients in order to bring the serum carbon dioxide back to normal. Those 12 patients had a variety of metabolic disturbances; the authors added the total sodium bicarbonate requirement and divided it by the number of cases. That figure was then used in a formula employed as a means of estimating the required sodium bicarbonate needed in any patient to bring the carbon dioxide content to a normal amount.

Inquiry into the original paper shows that the variation per patient according to his state and disease was great, so that the equation derived from the averages could not be highly significant. The reason that this point is pertinent today is that all these calculations really resulted in an extremely large dose of sodium bicarbonate, and I believe that the data now being accumulated will certainly show that those excessively large doses of sodium bicarbonate have caused a large amount of sodium to go into the cells. Dosage should not be given according to the amounts calculated by these two methods.

The more I watch my patients and the more I learn from such work as that contributed by Dr. Darrow, the more convinced I am of this.

DR. GEORGE M. GUEST, Cincinnati: After Dr. Butler's remarks I wish to note that my co-workers and I in Cincinnati do employ the formula originally developed by Van Slyke for calculating approximately the dosage of sodium bicarbonate required for the correction of acidosis and that we believe the formula to be helpful. Actually, we usually administer only about one-half the dose calculated to restore the bicarbonate of the blood to a normal level, expecting that in most instances after partial correction the patient will make the final steps of readjustment without extra alkali, if all goes well.

The main thesis in Dr. Nelson's paper is concerned with the controversial question of whether recovery from acidosis in all phases is hastened by the administration of sodium bicarbonate; on this point I should like to offer arguments in agreement with those of Dr. Nelson. With regard to the chemical pathologic changes of acidosis, it is to be emphasized that the functional and morphologic integrity of the cells of the body are dependent on enzymatic reactions and that most of the cellular enzymatic reactions are pushed in the direction of breakdown of organic materials by a shift of p_H below normal. Restoration of the organic cellular constituents is hastened when the p_H of the body fluids is brought to the normal range, favoring enzymatic synthesis. That, I believe, may be offered as the strongest argument in favor of quick correction of the acidosis of diabetic coma as well as of acidosis resulting from diarrhea and other conditions in infants as discussed by Dr. Nelson in connection with his experimental studies.

DR. DANIEL C. DARROW, New Haven, Conn.: In the calculation of the dose of bicarbonate, I think you have all appreciated the implications of what I showed in the slides, that is, that in any given case the physician does not know whether there is an excess of sodium in the cells or whether there is a deficit.

I wrote a paper a few years ago in conjunction with Drs. Da Silva and Stephenson, in which we showed that a chloride acidosis produced by protein milk powder led to a loss of practically all the sodium that is normally in the cells. If one adds that amount of sodium to the amount of sodium that is necessary to raise the bicarbonate concentration in extracellular fluids to normal, one comes to about the calculated dose of a bicarbonate that Dr. Hartmann has used and that he has shown does restore the serum bicarbonate. However, if those cases that I have shown are recalled it will be seen that some of those patients already had an excess of sodium in the cells.

Now, if one institutes therapy with potassium, as I believe one should, and if one continues to use the doses of bicarbonate that are calculated as recommended by Hartmann, one then will be giving, obviously, too much bicarbonate. I think, therefore, that this whole question will have to be reexamined, taking into account the exchange of sodium and potassium across the cellular membrane as well as the deficits of sodium in the extracellular fluids.

DR. WALDO E. NELSON, Philadelphia: I think that Dr. Butler's question has been answered, perhaps better than I could answer it. I should like simply to add that the calculation methods for determination of the alkali dose which we have employed in this study and have used clinically have from clinical experience been adequate to avoid the production of alkalosis.

As Dr. Guest pointed out, it has been the practice, I think, of a good many of us in the treatment of diabetic acidosis to attempt correction only up to 35 or 40 volumes per hundred cubic centimeters and permit other factors to account for the rest of the correction.

Whether or not the correction of the acidosis with alkali and the administration of the saline solution provide an adequate means for restoration of other electrolytes is another question. In this respect I cannot add to Dr. Darrow's comments.

Dwarfism in Healthy Children: Its Possible Relation to Emotional, Nutritional and Endocrine Disturbances. DR. NATHAN B. TALBOT, DR. EDNA H. SOBEL, BERTHA S. BURKE, M.A., DR. ERICH LINDEMANN and SHIRLEY B. KAUFMAN, M.S., Boston.

A sizable number of physically sound but abnormally small children have been encountered. It was noted that some were grossly underweight for their height and that the great majority appeared to have scanty stores of subcutaneous fat. Nutritional surveys revealed that while their intake of building materials, such as protein, was not apparently inadequate for growth, their total caloric intake did appear to be undesirably low. In the majority of instances this predominantly caloric malnutrition appeared to be related to anorexia secondary to emotional disturbances. Correction of emotional difficulties has resulted in an improvement

in appetite which has been followed in turn by a rapid gain in weight and an appreciable increase in the rates of growth and maturation.

While malnutrition per se may have been responsible for the slow growth, there were reasons to believe otherwise. A few children failed to resume normal growth when the dietary inadequacies were corrected. Furthermore, it was found that the growth rate of poorly nourished as well as well nourished dwarfs could be increased decidedly by the administration of a protein anabolic or growth factor, namely, methyl testosterone, without any evident change in diet. In a few well nourished dwarfs growth continued spontaneously at a satisfactory rate after one or two short courses of therapy with testosterone. These observations coupled with the evidence of the literature concerning the importance of anabolic endocrine products and especially of the pituitary growth hormone, as determinants of the rate of growth during childhood suggested that the dwarfism in this group of children may have been due to a functional hypopituitarism secondary to the limited caloric intake. If this supposition is correct, it might be assumed that this hypopituitarism reflected a homeostatic, or adaptive, reaction to the malnutrition.

Mention probably should be made of the alternative idea that malnutrion and/or emotional disturbances might have induced an overproducton of antigrowth factors by the adrenal cortex (the "S" hormone of Albright). This seems a relatively unlikely possibility. While still other explanations for the retarded growth of the present patients might be considered, this one seems inappropriate at present.

Thus retarded growth in otherwise healthy children may be an ultimate manifestation of a series of interrelated disturbances: (*a*) emotional difficulties resulting in anorexia, (*b*) anorexia resulting in malnutrition, (*c*) malnutrition resulting in hypopituitarism and (*d*) hypopituitarism resulting in retarded growth. In the presence of emotional anorexia it is difficult to improve the nutrition. When psychotherapy leads to an improved appetite, it becomes possible to provide a diet which contains a surplus of all the essential nutrients. It appears undesirable to use a substitute growth factor, such as methyl testosterone, before making an attempt to induce an acceleration of the rate of growth by proper feeding. However if adequate nutrition results only in gain in weight and fails to prompt a spurt of growth, a few short, intermittent courses of methyl testosterone may be useful, not only because the drug acts as a growth factor but because it may stimulate intrinsic mechanisms of growth.

If the problems presented by dwarfism in apparently healthly children gain wider attention, the purpose of this paper will have been fulfilled.

DISCUSSION

DR. HAROLD C. STUART, Boston: I have been following these studies of Dr. Talbot with considerable interest to see what application they might have to a somewhat different group of children that are usually considered to be within the range of normal persons.

Dr. Talbot has been studying children who are considered to be true dwarfs, chosen on an arbitrary basis of extremely short stature and therefore representing an extremely small percentage of the child population. He has presented some intriguing hypotheses as to the course of events which may have led up to the extreme dwarfing in these instances.

Any one who is following a relatively large series of so-called normal children will recognize that in the lower range of such a series there are always some who are nearly as small as these patients but who are not classified as dwarfs because they happen to be slightly too tall. My co-workers and I are studying a group of such children and although we have unfortunately not been able to have the careful psychiatric studies conducted by Dr. Lindemann, we have been observing their behavior. It is quite apparent that in some of these children there have been long periods of emotional disturbance due to environmental and familial factors. Now that we have this evidence, we hope to go further with a study of some of them from this aspect. Mrs. Burke, who made the dietary studies in this group for Dr. Talbot, has also been making similar dietary studies of our children, and

she finds that for a number of them the deficit in calories according to normal standards for age is approximately the same.

Dr. Talbot has pointed out that on a decidedly low caloric intake some children presumably will grow normally and will maintain normal pituitary activity; others will have a somewhat retarded growth, while still others will show interference with growth. It would seem safe to postulate that within any group of so-called normal children, such as I have mentioned, there are some that have had the same factors operating and affecting each child in the same way but to a different degree. I believe this gives wider scope to the importance of Dr. Talbot's work in recognizing the processes that may be operating and the management which has seemed to be effective, for the same kind of attention may be required by many more children of the type I have mentioned.

It is characteristic of the situation in the United States that the majority of children who take low caloric diets do so on the basis of appetite or habit or emotional factors. I should like to call attention to two rather more theoretic possibilities for the application of the studies which Dr. Talbot has reported. The children in some countries of the world are considerably smaller than children in the United States, and in general the diets of the people in these other countries, whether because of custom or of lack of food, provide smaller caloric intakes, especially in early life. It may be that when children are constantly on small dietary intakes there is a tendency for an adaptation on the part of the pituitary gland to take place to provide for slower growth and hence to make the intake of food relatively more adequate. That may account for the fact that when families of these nations migrate to this country their children born in this country become more like those of our nation.

Another possible application of these studies is in regard to the famine-stricken areas of the world today. There is still disagreement as to whether the prolonged underfeeding of many children during the war, according to American standards, has interfered with their growth, but it was obvious that the small numbers of children in France about whom I had an opportunity to obtain data over a period of two or more years were not growing according to expectancy for age. It may be that, with the greatly reduced caloric intakes resulting from restrictions of war or conditions of famine, there is again an adaptation on the part of the pituitary gland which is intended to protect children from nutritional disease but which will limit their growth if in effect over a sufficient period of time.

I think Dr. Talbot's study is an excellent example of what can be accomplished by taking some group of patients with an extreme form of a disease and studying them carefully and then trying to apply the results to less extreme situations.

DR. JULIAN D. BOYD, Iowa City, Iowa: I was happy to hear Dr. Talbot's report. My associates and I have been working clinically along similar lines, but have not had the opportunity to make controlled studies as he has.

Two or three comments seem particularly worthy of emphasis in regard to the appraisal of growth and the program for growth promotion. One deals with the complacency which the average physician holds in relation to a given child's physique and his ready assumption that such physique probably represents the expression of genetic factors, without consideration of currently operative environmental conditions.

We have postulated that if a child's height is as much as one standard deviation below the average for other children of similar age in the same community, we should assume that adverse environmental circumstances are operative until we have proved to the contrary. Our initial efforts with such children are directed toward the improvement of the child's conditions of life. In many instances we have been able to improve the child's habits of nutrition and of general hygiene through outpatient facilities and have restored such children to better levels of growth.

It is unsafe to assume that substandard levels of growth are innocuous. The child who is notably undersized and who is expected by his parents and other associates to maintain the activity levels appropriate for a child of his own age is

prone to have chronic emotional fatigue as a consequence of the imbalance between his physique and his output. In such a child emotional feeding problems tend to develop; and with lessened intake of food a vicious cycle is established.

Frequently the physician or the dentist contributes to the child's state of undernutrition through the prohibition of sugar, starches or other calorigenic foods. Even though a child receives daily a diet which includes a quart of milk, an egg and liberal servings of meat, vegetables and fruits, he may have a caloric intake of 1,300 calories or less. Unless the physician studies carefully the child's customary eating practices, he cannot be assured that nutritional factors are optimum for his patient.

Most nutritionists support the concept that obesity is due basically to the overconsumption of food. As a corollary, I believe that we should assume that substandard rates of growth are dependent on current faults of nutrition or of assimilation, until some other specific cause has been established. Many of our patients need betterment of their nutritional practices; but few of them require endocrine therapy.

DR. LAWSON WILKINS, Baltimore: I was much interested in Dr. Talbot's paper and also in Dr. Boyd's comments. I think all pediatricians have been faced with this problem and have not paid sufficient attention to it. I feel there is no doubt that these stunted or dwarfed children usually consume a diet low in calories and perhaps sometimes in protein.

The question I wish to raise is whether one is uniformly justified in excluding constitutional differences in the impulses of growth as a cause of the stunting and also of the poor appetite—in other words, where shall one put the cart and where shall one put the horse in some of these cases of poor appetite? I am sure that the normal child could be stunted in his growth by having a low caloric intake. But is one justified in saying that the impulse of growth actually may not vary in many of these children and that a defective impulse of constitutional or genetic origin might not account for the difference in height? Is it not possible that a child who constitutionally is growing at a slow rate may have less need for food and accordingly have a poor appetite and a small caloric intake? There is evidence that the appetite and the food intake may depend on the rate of growth rather than the reverse in the fact that when a spurt of growth is brought about by the administration of testosterone there is immediately a striking increase in the appetite.

I feel that to prove that the stunted growth in a particular case depends on a low dietary intake one must be able to demonstrate that by increasing the diet to a higher caloric level the rate of growth can be definitely accelerated. Dr. Talbot demonstrated this in 1 case shown in his slide, but failed to do so in other cases. I think, however, the point that Dr. Boyd brought out that other races subjected to an increased caloric diet grow with greater rapidity does show that diet has some influence on growth. I am loath to give up the idea, though, that there are real constitutional differences in the growth impulse, and I do not believe that all dwarfed children who have no endocrine disturbance could be made to reach average height if a high enough diet could be administered. Dr. Talbot at the end comes back to admitting such constitutional differences on the hypothesis that the response to the pituitary growth hormone is different in different persons.

I should also like to question Dr. Talbot's implication that the influence of testosterone on growth is through an influence on the growth hormone of the pituitary gland. It is not certain that the influence of androgen on protein anabolism and on stimulation of growth is the same as that of the pituitary growth hormone. These may act in entirely different ways. We know that the thyroid gland is necessary to activate the effects of the pituitary gland in early life, and we know that androgen is probably a factor in the adolescent spurt of growth which often is striking.

Dr. Talbot is quite right in emphasizing the importance of diet in growth, and his studies are valuable. At the same time I do not think he means to give

the impression that there are not constitutional differences in growth on a genetic basis or would refuse to admit that there may be a genetic type of dwarfism which sometimes may occur sporadically and sometimes in families.

DR. SAMUEL Z. LEVINE, New York: I should like to ask two questions: First, after the administration of methyl testosterone, for how long a period have the children been followed? It is conceivable that methyl testosterone might cause a prompt and fairly rapid increase in the rate of height gained without necessarily accelerating eventual growth in stature. The question arises whether testosterone per se, as Dr. Wilkins pointed out, may not have a deleterious effect on the hormone of the anterior lobe of the pituitary gland if given for sufficiently long periods of time.

The other question is whether testosterone propionate would have the same effect as methyl testosterone, since the methyl fraction of methyl testosterone plays such an important part in the transamination of certain of the essential amino acids.

DR. NATHAN B. TALBOT, Boston: I have no comments to make on Dr. Stuart's comments and really none to make on Dr. Boyd's except to say that I agree with both of them.

The comments of Drs. Levine and Wilkins can be considered perhaps more or less together. The administration of testosterone which was described in the paper proper was undertaken in order to answer a specific question, namely: Could these children be made to grow without any other therapy? The answer appeared to be "Yes."

Time did not permit the presentation of other data about some of these children. Perhaps they can be summarized briefly.

I mentioned that some children who had apparently undergone a period of severe malnutrition failed to resume a satisfactory rate of growth after the nutritional status had apparently been restored to normal. To such children we have given intermittently methyl testosterone over periods of three months with three month vacations between. In about 5 such patients it was noted that while testosterone induced a rapid spurt of growth during the first period of its administration and while the rate of growth may have returned to control levels on its discontinuation for the first time, after the second or third courses of testosterone the rate of growth did not revert to control levels, but it remained at at least a normal level. Thus, during the course of testosterone therapy processes of spontaneous growth appear to have become awakened. Though it cannot be said yet that there is a definite causal relation between this awakening and the therapy, the phenomenon has been observed sufficiently often to make us wonder whether testosterone may have a dual influence on growth: first, as an anabolic hormone directly to promote growth, and, second, as an agent to stimulate the anterior lobe of the pituitary gland to greater adolescent activity. The first action is reasonably authentic; the second is more speculative.

Dr. Levine's query about the prolonged use of testosterone is pertinent. Testosterone is capable of causing decided acceleration of skeletal maturation, especially when given over long periods of time in large doses. When the product causes precocious epiphysial closure and thereby shortens the duration of the growth period, it may well have defeated the purpose for which it was given. It is for that reason that we like to give testosterone intermittently, determining periodically whether or not the child can grow spontaneously. We also try to avoid giving testosterone to the point where skeletal acceleration as measured by osseous age exceeds acceleration of growth as measured by height age.

We have no information, I am sorry to say, on the use of testosterone propionate for the present series of patients. However, for other patients we have noted that testosterone propionate induces at least the same immediate growth response that is seen when methyl testosterone is given.

Congenital Anophthalmos: A Clinical Study of Early Mental Growth.
DR. ARNOLD GESELL, New Haven, Conn.

This case of congenital anophthalmos is noteworthy for two reasons. It presents one of the rarest of medical anomalies in an otherwise completely and superbly normal child. Congenital and neonatal blindness is usually associated with complications which make it impossible to assess accurately the developmental consequences attributable to visual deficiency alone. In the present instance one can observe clearly the effects of blindness on the patterning of infant behavior. Detailed observations and cinema records of behavior were made at the Yale Clinic of Child Development at the ages of 16, 28 and 40 weeks and of 12 and 18 months.

The subject, a boy, is physically well developed and except for minor infections has had an uneventful health history. His birth was normal; the birth weight was 8 pounds, 15 ounces (4,075 Gm.); he was breast fed. His cranium and facial features are well formed. He makes an agreeable impression despite the depressed orbits, diminutive and closed eyelids, scanty eyelashes and somewhat impassive countenance. The puncta and lacrimal glands function. Palpation of the orbits indicates an underlying soft, amorphous mass. No response to strong illumination can be elicited.

To what extent does complete blindness distort and retard behavior? Systematic developmental examinations supplemented by interview and documented by cinema showed a remarkable approximation to the ontogenetic sequences characteristic of the seeing infant. A favorable prognosis was made on the first examination, when the child was 16 weeks of age, on the basis of gross motor control, manual coordination, vocalization, attentive listening and general emotional tone and drive. The prognosis was strongly confirmed at 28 weeks and at subsequent examinations.

Despite blindness and without specific training, the basic patterns of body posture, manipulation, locomotion, exploitation and adaptive behavior took progressive form, thus establishing conclusively the fundamental role of maturation in the organization of the action system. Conditioning and learning play a secondary directive role. The retardative effects of blindness, per se, are readily overestimated.

The developmental course and deviations of behavior patterns are demonstrated with the aid of the cinema—with comments as to guidance measures and preventive mental hygiene.

DISCUSSION

DR. MARIAN C. PUTNAM, Boston: I thought this film was intensely interesting; I have one or two questions to ask Dr. Gesell. It is clear that certain forward steps in the child's development—or new achievements—took place in response to stimuli which he by chance produced and then felt the urge to reproduce. Scratching the table for the first time, for instance, presumably stimulated him to repeat the scratching. I should be interested to know whether Dr. Gesell feels that this child would have walked if he had not been placed in the standing position.

I have often wondered at what points a child's development is principally dependent on what he sees around him or on experiences as goals to be emulated in one way or another. Am I right, Dr. Gesell, in recollecting that you once said that the wolf children did not walk on their hindlegs but on all fours? If this child had not been encouraged by the parents to do so, would he necessarily have walked?

DR. ARNOLD GESELL, New Haven, Conn.: The concept of maturation does not deny the importance of environment. Development cannot take place in a vacuum. We need air to breathe; but the air can scarcely be called the cause of breathing. Breathing as behavior emanates from within. We must always assume at least a minimum of "environment"; but maturation is the primary factor because the environment cannot engender the basic sequences of development.

So, in locomotion the environment can influence the eventual patterns. I suppose that in an acrobatic environment children could be taught to walk on their hands. Even so their motor development would follow certain natural ontogenetic sequences.

For this reason, we may say that training cannot transcend maturation. Or, as Emily Dickinson put it: "Growth of Man, like growth of Nature, gravitates within. Atmosphere and sun confirm it, but it stirs alone."

The Syndrome of Ovarian Agenesis and Dwarfism. DR. LAWSON WILKINS and DR. WALTER FLEISCHMANN, Baltimore.

Ovarian agenesis is not very rare; we have encountered 13 cases in the past three years. In these girls the ovaries do not develop beyond the stage of the primitive genital ridge. No primordial germ cells are present, and the germinal epithelium does not proliferate. In place of the ovary there is merely a slender white streak in the broad ligament composed of stroma-like cells. The vagina, uterus and tubes are normally formed but remain infantile because of lack of estrogen. The breasts never develop. However, pubic and axillary hair develop due to the relatively normal production of androgen by the adrenal gland. It is probable that the defect is due to a genetic mutation. There are a number of other genetic defects commonly associated. The authors believe that the dwarfing is of genetic origin and cannot be explained by an endocrine dysfunction. Other defects which are frequently, but not always, associated are webbed neck, coarctation of the arch of the aorta and abnormalities of the muscles of the eyes.

The condition should be suspected when a dwarfed girl shows complete lack of female development, but there is development of pubic hair. The diagnosis can be confirmed by finding a high urinary excretion of a follicle-stimulating hormone. The differentiation between ovarian agenesis and pituitary dwarfism with sexual infantilism is discussed.

DISCUSSION

DR. JOSEF WARKANY, Cincinnati: I should like to ask Dr. Wilkins if substitution therapy with estrogens is helpful in these cases.

DR. LAWSON WILKINS, Baltimore: Dr. Warkany, I wonder whether Dr. Park put you up to starting me on the story of the "synthetic bride." But the synthetic bride did not have ovarian agenesis; she had pituitary infantilism.

The physician cannot make these patients with ovarian agenesis grow much, because their epiphyses are nearly fused when he sees them. By substitution therapy with estrogen one can do a great deal for them and can change them from sexually infantile children into small adults having nearly normal female sexual characteristics except for fertility. They consult one at the age of 17 to 20 years or older, discouraged with life and all that life may hold for them. Ihave seen some of them when they had engagement rings and were about to be married. They are usually exceedingly morbid, worried and discouraged, especially about the lack of sex development. They wear padded brassieres. We can do a great deal for them in turning them from sexually infantile dwarfs into small but otherwise normal-looking women. We first start substitution therapy with diethylstilbestrol. Usually this is given continuously for a period of six to twelve months, unless uterine bleeding occurs sooner. They receive 1 mg. of diethylstilbestrol daily, or sometimes 0.5 mg. The breasts develop rapidly. At the end of that time the uterus and vagina are practically of adult size. It is then important to give interrupted cyclic estrogenic therapy to allow endometrial breakdown; otherwise, endometrial hyperplasia may occur with bleeding from that. So the scheme adopted by my associates and me is, after we have developed them to a certain extent, to give cyclic therapy. We introduced progesterone in that therapy, because we want to simulate the normal endocrine setup of the menstrual cycle as much as possible and because we feel it likely that progesterone as well as estrogen has some influence on mammary development. The routine is to give diethylstilbestrol alone for two weeks; diethylstilbestrol plus progesterone, which we use in the form of

anhydrohydroxyprogesterone (Lutocylol) by mouth, for a week, and then no treatment for a week. The patients menstruate regularly on withdrawal of treatment. Some menstruate two days after it is stopped, some regularly three days after it is stopped, and some regularly four days. There are varying amounts of blood for three or four days, and then the whole cycle is resumed again.

The appearance of these girls is greatly improved, but the psychologic improvement is most striking and well worth while. They feel that they are normal women. The question of marriage has come up. They are told that they cannot possibly have children and that it would not be fair for them to deceive any one into thinking that they were normal women, but that if the opportunity for marriage presents itself and the condition is explained to the prospective husband, normal marital relations would be possible, as they are anatomically and physiologically like other women except for their inability to bear children.

Basal Metabolism of Children: Critical Interpretation Based on Observations in Obese Subjects. DR. DONOVAN J. MCCUNE and DR. HILDE BRUCH, New York.

Aside from obvious technical errors which may invalidate the results, the so-called basal metabolic rate—better designated as the basal metabolic quotient—contains interpretative assumptions which frequently make it deceptive. This criticism is exemplified by the discordant results in obesity. There is conspicuous discrepancy among various calculations using height, weight and surface area, and the discrepancy increases in amount as the excessive weight becomes greater. Hypothesis plays a considerable role in the attempt to regularize the results. The critical difficulty is lack of other measures of the active mass of the body. While this can be estimated with satisfactorily reliable precision in persons of average cellular composition, it is virtually impossible to predict in persons whose proportions are anomalous.

These points are strikingly illustrated by the case of a greatly overweight boy who was studied during the course of a therapeutic reduction of weight.

DISCUSSION

DR. HARRY H. GORDON, New York: I should like to register a vigorous dissent to Dr. McCune's conviction that determinations of basal metabolism are not of importance or of aid in treating patients with obesity. I think, in the first place, we will both agree that the oxygen consumption of obese children on One Hundred and Sixty-Eighth Street is the same as that on Sixty Eighth Street. It comes down, then, to a question of interpretation of the data, and part of the confusion is derived from the use of multiple standards. Actually, if one takes one standard and measures the metabolism in enough patients, one ultimately gets a "feel" for the data which permits their use in the management of a child with obesity.

When the New York Hospital first began to operate on Sixty-Eighth Street, Dr. Du Bois gave Dr. Levine carte blanche to use any standards he wanted for children in place of the Du Bois standards, which had been derived from observations on only a few children. After a careful survey of the literature, the Bierring standards for boys were chosen because the report of this Danish investigator indicated that his observations had been carefully made. No similar standards were found for girls, and the Kestner-Knipping standards were finally chosen, after recalculation, because the observations of these workers for boys were closer to the Bierring standards than any others in the literature. From Dr. Washburn's Child Research Council group, Lewis and his co-workers have reported an adequate number of carefully made determinations on American boys and girls of normal stature, and these data should serve as standards of reference for basal metabolism.

As far as obese children are concerned, it probably does not matter whether one uses weight or surface area as a standard of reference. As Dr. McCune's data indicate, height is unsatisfactory, for obvious reasons. My associates and I prefer

surface area to weight because from a teleologic standpoint one has a right to expect that surface area, which conditions loss of heat, will also affect production of heat, in order to maintain body temperature. If teleologic reasoning is unsatisfying, then perhaps the idea that the rate of oxidation will be determined by surfaces within the body will lead to the choice of surface area as the standard of reference.

At any rate, using the standards of surface area mentioned, the basal metabolism was measured in most of our obese patients. The last time we made a count, about five years ago, there were determinations on approximately 400 patients.

At this point, I think Dr. McCune has a different opinion as to the value of the tests. In 4 of the 400 patients, about 1 per cent, the basal metabolism was low and responded to a small dose of thyroid, 2 grains (0.13 Gm.) or less, with a significant elevation. In 396 patients the test was of value not in diagnosing hypothyroidism but in giving the patients a little more reassurance that their salvation was not going to come from a pill and that they would have to settle down to the pretty grim business of dieting. Thus having chosen a standard and having used it consistently, we believe that the determination of basal metabolism has been of assistance. First, it points out the rare patients who require thyroid therapy, and we were not able to detect them clinically or by cholesterol tests; second, it helps us with the subsequent management of the other patients.

Dr. Nathan B. Talbot, Boston: My attitude toward the use of basal metabolism as an index of thyroid function may be summarized briefly. About five years ago it was given up at the Massachusetts General Hospital as an index of thyroid function because it was found to be unreliable even in children with clear-cut hypothyroidism. Perhaps one reason for this is that the thyroid gland is only one of several factors which determine the level of basal heat production. If the thyroid gland of a normal person is extirpated completely, his energy metabolism will fall only to about minus 40 per cent, the remaining 60 per cent being maintained by some other (X) factor or factors. From observations that Drs. E. J. Kepler and R. Rawson and I are in the process of collecting, it would seem that one can have hypothyroidism with a normal basal metabolic rate as a consequence of an increase in the X factor. Contrariwise, one may have thyrotoxicosis with a normal basal metabolism when there is a lowering of the X factor approximately compensating for the rise in the thyroid factor.

Such considerations as these have led us to rely on other indexes of thyroid function. I wonder whether Dr. McCune has come to any similar conclusion.

Dr. Alfred H. Washburn, Denver: I have not much to add to what Dr. Gordon said, but I am tempted to make a few comments about standards. It seems to me that Dr. McCune is asking the impossible of standards. If one uses a standard as a base line one becomes familiar with how far a given person departs from that base line. One uses one's experience to interpret what type the person is.

If one wishes to take a mode of reference that will bring most subjects closest to the base line so that there are approximately an equal number scattered above and below it, and if one is dealing with a heterogeneous group of subjects, the fat, the thin and those in between, then reference to surface area will be the closest to a midpoint.

I agree with Dr. Gordon, it is not so much a question of which standard one uses as it is of using a single standard and then becoming familiar with what type of subject departs in what way from that particular base line.

Dr. A. Ashley Weech, Cincinnati: I am greatly interested in the material which Dr. McCune and Dr. Bruch have presented because of certain theoretic considerations. The total output of heat of the human body can be looked on as the sum of the heat generated by all of the individual cells of the body. Some of these cells are located in what is spoken of as metabolically active organs, and some make up what are relatively inactive tissues. Thus one may think that the heart and the liver and the lining of the intestine are metabolically extremely active, while bone is inactive. In obesity the increment in weight is largely made

up of an intermediate type of tissue which is metabolically less active than organs like the liver and metabolically more active than bone. If the basal metabolism in obese children remains constant when expressed in terms of energy output per kilogram of body weight, it can only be an accident that the result should come out in this manner. One can think that the combination of muscle and fat which makes up the increment represents a figure near the average of that derived from the more active and the less active tissues, and if this is so the gain in weight should not affect the per kilogram figure.

DR. SAMUEL Z. LEVINE, New York: In the last chart, Dr. McCune showed that the metabolism of a fat child was 2,300 calories when the youngster weighed 112 Kg. and was 1,900 calories when the child weighed 82 Kg. The discrepancy is in accord with expectation. One does not need to postulate that the drop in weight proves that fat is not inert tissue. Obviously, a person weighing 112 Kg. requires more calories to cover his metabolic needs than when his weight has fallen to 82 Kg.

DR. DONOVAN J. MCCUNE, New York: This discussion suggests that pediatrics has found a bone of contention to take the place of infant feeding. It also suggests that probably the best solution would be to refer the matter to a committee.

I have no effective rebuttal of the criticisms except to point to the difference of opinion which has been expressed. Personally, I have some misgivings regarding the use of standards which require a craftsman's familiarity with them plus a certain amount of virtuosity to employ them effectively in clinical practice —as Dr. Gordon has suggested and as Dr. Washburn has, I believe, seconded. Dr. Levine, it seems to me that we do not mean the same thing. You said more oxygen was utilized by a fat person than by a thin one. That, to me, is the calorigenic effect of fat. Did you mean simply that more heat is required to propel blood through that fat?

DR. SAMUEL Z. LEVINE, New York: Yes.

DR. DONOVAN J. MCCUNE, New York: That could be. I do not know enough about it to be sure. I had in mind the various demonstrations of exchange of isotopic material with the fat store, and I should have thought that they indicated that fat is not metabolically inert.

DR. SAMUEL Z. LEVINE, New York: As an indication, the blood pressure is invariably high when the patient is overweight.

DR. DONOVAN J. MCCUNE, New York: Measured with a wide cuff.

DR. SAMUEL Z. LEVINE, New York: Yes. And the blood pressure drops with the same cuff when the weight drops, so that the heart must have been working harder.

DR. DONOVAN J. MCCUNE, New York: I will concede that.

Penicillin in the Treatment of the Syphilitic Infant. DR. ELIZABETH KIRK ROSE (by invitation), DR. PAUL GYÖRGY and DR. NORMAN INGRAHAM, JR. (by invitation), Philadelphia.

Thirty-six infants with congenital syphilis were treated with penicillin administered intramuscularly in dosages ranging from 11,000 to 50,000 units per pound of body weight (24,200 to 110,000 units per kilogram) over periods of seven to fifteen days. Eighteen have become clinically normal and seronegative. Four are clinically normal, but 3 of these are seropositive and 1 has a doubtful reaction. Seven died; 2 have been lost to follow-up, and 5 have been treated too recently for any evaluation except that of immediate reaction to treatment.

(The amount, duration and gradation of dosage are discussed. Details of the fatal cases are explained. Emphasis is placed on the specific pediatric implications of therapy for the infant with syphilis.)

DISCUSSION

DR. J. C. PETERSON, Nashville, Tenn.: I should like to ask Dr. György one or two questions and to add some comments.

I wish to emphasize the necessity of treating the patient for at least the time stated to be optimum. I think this should be stated as the minimum period of treatment rather than as the probable optimum time. Also, the highest doses of penicillin recommended are in line with what we have found in our limited experience to be satisfactory.

I should like to ask Dr. György if he and his co-workers had cultures of blood from their infants. We have found that syphilitic infants frequently have severe secondary bacterial infections and often unsuspected staphylococcic sepsis. I suspect that some of the roentgen findings reported might be based on that infection rather than on syphilis.

DR. EDWARDS A. PARK, Baltimore: I think that the experience with the penicillin treatment of congenital syphilis at the Harriet Lane hospital has been the same as that which Dr. György described. I was extremely interested in Dr. György's roentgenograms (he was kind enough to show them to me before the meeting), and I was unfamiliar with the sudden appearance following treatment of these enveloping shadows at the end of the shaft. I think I have probably seen similar shadows, and they have never been bright enough for me to appreciate their significance.

Both in congenital syphilis and in scurvy, the osteoblasts seem to be affected in such a way as to be unable to produce bone. For instance, on the framework of the matrix substance of the cartilage, which is completely calcified in both scurvy and congenital syphilis, the osteoblasts do not produce bone.

I suppose the phenomenon which Dr. György pointed out in the healing of syphilis is explained by the fact that when the spirochetes are killed the osteoblasts regain their activity and produce bone at an enormous rate. I do not believe that those shadows are produced by calcification. Their appearance indicates that it was metaplastic bone which was formed. Dr. György made a comparison to scurvy, and I think his comparison was an exact one. All these lesions which one saw in Dr. György's roentgenograms could be explained by syphilis. I do not think there is any reason to conjecture on the pyogenic effects in addition.

DR. CHARLES HENDEE SMITH, New York: I should like to ask a question. Dr. György suggested 70,000 units per pound, but he did not say whether it was 70,000 units per dose or per day.

DR. PAUL GYÖRGY, Philadelphia: The total dose of 70,000 units per pound represents the amount of penicillin given over the total period of fifteen days. It has to be divided by 120 and multiplied by the total weight of the infant (expressed in pounds). Thus, one obtains the single dose given every three hours for fifteen days. In the future, it probably will be advisable to increase the doses further.

In answer to Dr. Peterson: It is improbable that widespread osteomyelitic lesions in almost all long bones seen in the infants under treatment could have been due to pyogenic osteomyelitis.

I am grateful for Dr. Park's remark. We were not sure whether the calcification—or ossification, as he calls it—was due only to the activity of the osteoblasts or whether there was some calcification in the surrounding soft tissue. We accept Dr. Park's opinion as to the osteoblastic (periosteal) origin of the calcification observed, in analogy to the healing in scurvy. More study is needed to establish the real nature of these intensive calcium deposits appearing in young syphilitic infants being given penicillin treatment.

Benign Histoplasmosis and Pulmonary Calcification. DR. AMOS CHRISTIE, and DR. J. C. PETERSON, Nashville, Tenn.

For a number of years one of the unsolved problems in the control of tuberculosis has been the question of calcifications in the chests of persons who do not react to tuberculin.

In a recent paper we reviewed the extent of the problem and outlined the clinical and epidemiologic evidence for suspecting a benign form of histoplasmosis or some other closely related infection to be the cause of the phenomenon.

In this paper we wish to elaborate further on this thesis by summarizing our experience with cutaneous tests using a broth culture filtrate of Hemophilus capsulatum. The age and geographic distribution of the sensitivity are reported, and we wish to add pertinent comments concerning the specificity of the antigen.

Tests with histoplasmin and tuberculin were given to 1,488 residents and 644 nonresidents of Tennessee. Each subject was examined by a roentgenogram of the chest.

Analysis of this material revealed the following interesting facts.

1. There were three times as many children showing pulmonary calcification as reacting to tuberculin.

2. Of those with calcification in their chests, 87.4 per cent are sensitive to histoplasmin, while only 18.8 per cent of the calcifications are associated with tuberculin sensitivity.

3. Study of the group by age reveals what seems to be a cause and effect relation between the rate of development of sensitivity to histoplasmin and calcification, which does not exist between calcification and the rate of development of sensitivity to tuberculin.

4. Study of the geographic distribution of calcification and of sensitivity to histoplasmin reveals that where a prevalence of sensitivity to histoplasmin is high the prevalence of calcification is high.

The evidence to support our ideas concerning the specificity of the antigen is reviewed.

(*a*) Infected animals become sensitive to histoplasmin. No one reacts to the broth.

(*b*) No one reacts to histoplasmin on the West Coast unless he has been infected with coccidioides, and then only equivocally.

(*c*) No one in this area reacts to coccidioidin or to haplosporangin.

(*d*) The age and geographic distribution of sensitivity to histoplasmin as reported supports the idea that the antigen is specific.

(*e*) There is a constant relationship between sensitivity to histoplasmin and pulmonary calcification, a demonstrable pathologic lesion. Our studies show that 87 per cent of those who have pulmonary calcification react to histoplasmin, while only 48 per cent of those not showing calcification have been sensitized to the antigen. Benign forms of histoplasmosis have been pathologically demonstrated, and a summary of this point is contained in the paper.

It seems quite certain that in states bordering on the western bank of the Mississippi River and in the states of the Western Appalachian slope, a large part of the pulmonary calcifications are due to some infection other than tuberculosis. Our studies indicate that the same relationship may have a much wider application.

If these studies have no other value, they do serve to reinstitute and reemphasize the necessity of employing tuberculin tests or demonstrating tubercle bacilli in establishing the diagnosis of tuberculosis in minimal and noncavitating pulmonary lesions and in the healing lesions with pulmonary calcifications. Present day concepts of the primary complex, or first infection tuberculosis, in relation to pulmonary calcification need reevaluation.

DISCUSSION

DR. JOHN CAFFEY, New York: Dr. Christie has kept me informed on the progress of his work during the last several months, so that I have had the opportunity of studying it in detail. The validity and the significance of the data depend almost entirely on the specificity of Dr. Christie's antigen for histoplasmosis used in cutaneous testing. The specificity has been studied from several angles, and it seems to me that the evidence is conclusive that the antigen is specific. The geographic distribution of the positive reactors, the age distribution of the positive reactors, the high correlation of positive reactions with massive calcification in the lungs of subjects who are negative reactors to tuberculin—these all point to the

specificity of the antigen for histoplasmosis. It should be emphasized that the intrathoracic calcifications with the highest correlation are the larger ones—that they are not small shadows in the hilar regions which may be and are commonly confused with calciferous lesions when they are actually cast by the larger blood vessels projected axially.

The authors have shown that histoplasmosis is an important disease, both as a clinical entity and as a public health problem. Their data indicate that it is usually a primary infection of the lungs with early and late dissemination to many other tissues. In these respects it resembles tuberculosis. Their findings are of the greatest importance in the differential roentgen diagnosis of calcifying diseases of the lungs and intrathoracic lymph nodes. In some parts of Tennessee and probably in many other regions, calcifying intrathoracic histoplasmosis is more common than calcifying intrathoracic tuberculosis. It is now manifest that in a large portion of the United States intrathoracic calcifications demonstrated roentgenographically can no longer be assumed to be of tuberculous origin but must be interpreted in the light of cutaneous sensitivity to tuberculin, histoplasmin and coccidioidin. In the cases in which a patient reacts positively to more than one of these antigens, it seems doubtful that a conclusive diagnosis of the cause of intrathoracic calcifications will be possible. It is interesting to speculate on the possibility of multiple calcifying intrathoracic complexes in a single patient due to different causal agents: for instance, one due to tuberculosis, another to histoplasmosis and a third to coccidiosis.

The implications of the findings of Dr. Christie and Dr. Peterson from a prophylactic and a public health standpoint are of great import and warrant immediate consideration and action. Several of their observations suggest that histoplasmosis is a dust-borne infection of the respiratory tract and not a person to person droplet infection like tuberculosis and many other diseases of the respiratory tract. Special preventive measures will have to be worked out and applied.

The authors have said little about the early exudative phase of pulmonary histoplasmosis or about the incidence of erythema nodosum among their patients. Perhaps they will tell us something of the earliest phases of the disease in the discussion to come. I should also like to learn about the frequency of abdominal histoplasmosis. Prior to this work, in the few cases of the disease which were diagnosed at necropsy, the primary infection has apparently been located in the abdomen. Roentgen study of the abdomen might demonstrate intra-abdominal calcifications in the positive reactors to histoplasmin who do not show calcifications in the thorax.

I want to express again my admiration and to give congratulations to Dr. Christie and Dr. Peterson for their highly meritorious investigation of an important and hitherto poorly understood disease. Their presentation today will undoubtedly take its place in the front rank of the medical investigations of this decade.

Dr. Edwards A. Park, Baltimore: Dr. Christie's evidence of a circumstantial nature that histoplasmosis is the cause of these calcifications in children who do not react to tuberculin is most informative. I do not believe anybody who listened could help being tremendously impressed. It seems to me the circumstantial evidence is so formidable that Dr. Christie could stop trying to accumulate any more because further circumstantial evidence is never going to establish the fact; it may magnify the evidence, but it will never be proof.

I should think that now the crucial point is to study children at autopsy and determine the nature of the nontuberculous lesions in the lungs of these children who react positively to histoplasmin but do not react to tuberculin. Dr. Christie has already had a few such cases, but in areas such as the one in which he is working, in which the infection must be so prevalent, I should think it would be almost certain that the exact nature of the lesions could be established by autopsy studies.

Dr. Janet Hardy, Baltimore: I think that Dr. Christie deserves thanks for offering a solution to one of the knotty problems in tuberculosis. All physicians have been confronted with persons who have calcified lesions in their chests, who

do not react to tuberculin, who have never been sick and who have never had a history of exposure to tuberculosis. My associates and I have been familiar with Dr. Christie's work for some time. Dr. Peterson and he were kind enough to supply us with some of their antigen, which we have used to a rather limited extent.

Our studies of Dr. Christie's antigen have fallen into three groups. All the groups are rather limited, I am afraid. The first persons on whom we tried the antigen belonged to several family groups. These families were interesting to us because they contained from 4 to 7 children. There were four families, and most of the children in each family had calcified lesions in the chest; yet most of the children gave negative reactions to tuberculin.

We tested the family groups with histoplasmin and found that with the exception of the youngest child in each of three families, they, including the parents, were all positive reactors. These people were all from rural Maryland and had done field work.

Then we tried the antigen rather haphazardly in the outpatient department and in a series of about 90 tests found 18 positive reactions. We tried the antigen in the wards in the Harriet Lane Home. There the situation was a little different because many of the ward patients were very young; but in a group of 46 patients, we found only 1 positive reaction. This reaction was in a boy about 8 years old who had a negative reaction to tuberculin. When a roentgenogram was made in the light of the positive reaction to histoplasmin, he was found to have several calcified lesions in his chest. He had never been out of Maryland, but had lived in rural parts of the state.

We made one other study last fall which was carried out as a result of the findings of Dr. Christie and of Dr. Carroll Palmer. We studied a group of about 330 subjects, who are now between 15 and 30 years of age and who as young children had primary tuberculosis. What we wanted to find out from these persons was whether a loss of sensitivity to tuberculin years after a primary infection is possible. This group of 300 subjects have been followed for an average of almost fourteen years, and some of them for as long as twenty years. When they had primary tuberculosis, they were all sensitive to at least 0.1 mg. of tuberculin.

It is rather interesting that as children about 80 per cent of them had contact with persons known to have tuberculosis. This per cent may seem unusually high, but many of the patients were chosen from the oldest siblings of the children in the Harriet Lane tuberculosis clinic and from the Harriet Lane health clinic, which specializes in doing contact examinations on children exposed to tuberculosis.

When these subjects were restudied last fall, we did roentgen studies of their chests and performed tuberculin tests. They fell into three groups:

First, there was a group of about 60 persons who had had severe primary lesions as children; without exception they, on an average of almost fifteen years after the infection, were still decidedly sensitive to tuberculin.

The second group included about 170 subjects who had mediastinal tuberculosis and no lesions other than primary foci in their pulmonary parenchyma. At least 2 per cent of those subjects had become anergic to 1 mg. of tuberculin. Two of these 4 persons who became anergic had calcified lesions in their chests.

The third group of subjects consisted of about 80 persons who had reactions to tuberculin tests as their only manifestation of a tuberculous infection; 6 per cent of these had become anergic to 1 mg. of tuberculin.

I go into these details because I want to make a point. One reason for the continued sensitivity of these subjects might possibly be the fact that they come from an urban community in which the tuberculosis rate is rather high, but this fact can probably be excluded by comparing the degrees of sensitivity in the three groups. They all would have equal opportunity to acquire subclinical infections which might keep their sensitivity at a high level, and yet the three groups have behaved rather differently.

From these studies we are inclined to believe that most people who have had tuberculosis remain sensitive to tuberculin and that some explanation other than

tuberculosis for all this calcium seen in subjects who do not react to tuberculin is in order. Dr. Christie has offered an extremely satisfactory explanation.

DR. CHARLES HENDEE SMITH, New York: This geographic distribution of disease has always interested me. I remember a paper describing a number of cases of a condition in the Middle West, which was almost never seen on the seaboard, and which excited considerable controversy between different sections of the country about whether it really existed or not. Dr. Schick at that time pointed out the confusion of a German professor who moved from the Rhineland to East Prussia, where he found an entirely different set of diseases and where his former experience served him little.

I should like to ask Dr. Christie if lateral roentgenograms have been taken of many of his patients. Dr. Edith Lincoln pointed out at Bellevue a long time ago that calcification often shows on a lateral view which is missed entirely in the anterioposterior roentgenogram because it is superimposed on the central shadow of the vertebrae or the heart. Lateral views might show an even higher percentage of calcifications in histoplasmosis.

DR. AMOS CHRISTIE, Nashville: We are about through with the accumulation of circumstantial evidence, and are moving rapidly into the laboratory phases of the problem. I hope in another year to be able to tell something about the pathogenesis of the disease. It seems to have a portal of entry in the gastro-intestinal or respiratory tract in which ulcerative lesions are produced. I hope it was noticed how early the subjects in the young age group gain sensitivity to histoplasmin. It has been a clinical observation for a number of years that calcification also develops very early. In this early age group I think we have revealed a high incidence of atypical pneumonitis with lesions of the chest which we are following closely and which we think will go on to calcification.

Dr. Caffey asked about calcification in the liver and spleen. We have not taken routine roentgenograms of the abdomen, and we have not taken routine lateral roentgenograms. We have considered ourselves lucky in wartime to get so many anteroposterior views.

We have seen erythema nodosum, and I think constantly of Dr. Faber who, in his presentation from this platform about four years ago, described the benign form of coccidioidomycosis so dramatically. This San Joaquin Valley fever, which I also was brought up on, is a connecting link between the observations in California and the benign form of fungous disease here. We see erythema nodosum not infrequently in negative reactors to tuberculin and those having negative reactions to all other types of skin test material except histoplasmin. We have seen pleural effusions also, including bloody ones, which we think might be part of this picture.

I think you might be interested to anticipate at least what might be the origin of this fungous infection. We feel that it is a soil-borne or dust-borne fungus, and we have some evidence to support this. That problem, however, has not been entirely proved to every one's satisfaction with coccidioidosis, although I am quite certain in my own mind that it is dust borne or soil borne. Dr. Goodpasture has been urging us to explore the possibility that the dog population may be a means of transmission. Perhaps we shall be able to contribute to an understanding of this in a subsequent work.

Experimental Transmission of Japanese B Encephalitis by Mosquitoes and Mosquito Larvae. DR. HORACE L. HODES and DR. HERBERT S. HURLBURT, Baltimore.

In July 1945, an outbreak of encephalitis occurred on Okinawa. The Japanese B encephalitis virus was shown by means of the complement fixation test to be the cause of this outbreak. Evidence was obtained that horses as well as human beings were affected by the virus. Because mosquitoes had been suspected as the vector involved in the transmission of the disease, attempts were made in the laboratory to transmit the disease by these insects.

Mosquitoes of the species Culex jepsoni, Culex quinquefasciatus and Aedes vexans were employed. Adult females of these species were fed material containing the Okinawan strain of the Japanese B virus and kept at a temperature of 30 C. for seven to thirteen days. At the end of this time the mosquitoes were afforded the opportunity of biting infant mice. After an incubation period of six to eight days, symptoms of disease of the central nervous system developed in these mice, and a virus which was identified as the Japanese B encephalitis virus was recovered in each instance. Successful transmission of the disease was obtained with adult females of each of the three species of mosquitoes.

Experiments were also carried out to determine whether mosquitoes which were exposed to the Japanese B virus in the larval stage of their life cycle could on reaching adulthood transmit the disease to mice. Second and third instar larvae of the species Culex jepsoni were placed in water containing a 1:10,000 dilution of Japanese B encephalitis virus and kept there for eight hours. They were then washed with 5 liters of distilled water and placed in an incubator at 30 C. where they were permitted to complete their life cycle. After they emerged as adults, the females were given the opportunity of biting infant mice. In a number of the latter animals symptoms of disease of the central nervous system developed, and a virus which was identified as the Japanese B encephalitis virus was isolated from their brains. This experiment was repeated with the same result.

DISCUSSION

DR. FRANCIS F. SCHWENKTER, Baltimore: I really know little about this except that I was on Guam during the period when the experiments were being carried out and was able to observe them. One of the things that Dr. Hodes did not bring out is the extreme difficulty of working with these very tiny mice and of infecting mosquitoes experimentally. There was a great deal of technical perfection put into the work that he did. The question which has intrigued us most was what mechanism was used by nature to transmit the virus through the mosquito. When one thinks of the fact that the mosquito must inject, if he injects anything at all, a tiny volume into a mouse or into any animal that he bites, it must be either that the concentration of virus in the fluid injected is tremendous or else that the virus itself has some other qualitative factor which makes it much more infectious than virus in an emulsion of brain tissue.

I should like to ask Dr. Hodes whether he has any ideas on this subject.

DR. HORACE L. HODES, Baltimore: The interesting part of the problem, as Dr. Schwenkter has pointed out, is: What is there in the mosquito that apparently enhances the ordinary infecting capacity of the virus? There are two possibilities: one, that in the relatively undifferentiated cells of the mosquito the virus multiplies to an extent greater than it does in the mouse; the other, that the mosquito gets rid of certain inhibiting substances which in the mouse brain and in other mouse tissue prevent the full virulence of the virus from becoming apparent.

Probably the significant part of this is that one might be able to use mosquito larvae as culture mediums. It seems entirely possible that one may be able by passing viruses through mosquito larvae to infect mice, for instance, with viruses which ordinarily do not affect these animals.

The Initial Lesion in Poliomyelitis. DR. HAROLD K. FABER and ROSALIE J. SILVERBERG (by invitation), San Francisco.

Investigation of the inward passage of virus from the respiratory and alimentary mucosae toward and into the central nervous system in experimental animals and in 8 human beings in whom the disease was fatal revealed that the initial lesion is produced in the regional ganglions of at least four nerve systems (trigeminal, gustatory, visceral afferent and sympathetic) supplying superficial fibers to the mucosae named, with evidence of centripetal spread in their central connections, mainly in the pons and medulla, where the secondary lesions were found. Heavy and consistent lesions were also found in the reticular formation at the same levels.

Primary symptoms (first day) were tabulated from 85 cases of acute poliomyelitis, and a correlation between these and the localization of lesions in the brain stem was suggested: headache and sore throat with the trigeminal region, vomiting and nausea with the visceral afferent and spasm of the neck and back with reticular formation.

The most frequent portal of entry appears to be the pharynx and perhaps the upper bronchial tree.

DISCUSSION

Dr. John A. Toomey, Cleveland: I enjoy listening to Dr. Faber, especially when he speaks about the neurologic problems in poliomyelitis. None of us can disagree with him about the various ways virus may enter the central nervous system. He has given a clear picture of the many possible portals.

I wonder if he would care to comment on the fact that many of the older clinicians, and perhaps he himself, have noticed that in the years past the disease was in the majority of instances one involving the peripheral musculature rather than a disease of the bulb.

It seems to me that there is a definite change in the character of the disease from that which I knew in years gone by, in that now there is a decided increase in the bulbar and in the upper respiratory types. I wonder if Dr. Faber would like to comment on this.

Dr. Faber has commented on the ganglions, especially the celiac ganglions. I am also interested in this area, and I have tried to recover the virus from the celiac ganglions in 15 postmortem specimens and was successful in only 1. I believe that Sabin was also successful in recovering it from 1 patient.

In monkeys (Rhesus) we were able to show destruction of nerve cells in the ganglions, but when we examined control monkeys not given injections of virus we found the same type of reaction. As there is the possibility of subclinical laboratory infection in monkeys, I cannot say that the controls might not have been infected.

I should like also to have his comments on the work of Dr. Harbitz and Dr. Scheel. I read Faber's paper in the *Journal of Experimental Medicine,* of which this is a brief presentation, and Drs. Harbitz and Scheel's 13 cases of bulbar poliomyelitis were mentioned. I wondered why in 6 of those cases of so-called bulbar poliomyelitis there was no evidence of pathologic changes in the pons-medullary area.

I cannot quite agree with Dr. Faber's explanation of the spasm, because spasm also occurs in meningitis, any type of meningitis, and even in those patients who die no evidence of involvement of the basilar nuclei is found.

Has Dr. Faber noted any anatomic differences in these secondary neurons as they appear in his six illustrations of portal of entry and spread?

I wish to congratulate Dr. Faber on his lucid explanation of a particularly elusive problem.

Dr. Charles Hendee Smith, New York: I am interested in Dr. Faber's explanation of the signs in the neck and spine. I have always felt, as Dr. Toomey suggested, that the spasm is merely an evidence of meningism such as is obtained in many other conditions. It certainly has no relation to the paralysis, and in a fairly extensive experience with poliomyelitis I have never seen spasm in the paralyzed muscles or limb in the earlier stage.

Why does the spasm in the neck and spine disappear with the advent of paralysis in the leg or arm? I supposed it was due to the disappearance of meningism. How can that be reconciled with the finding of definite lesions in the reticular formation if these lesions are the cause of the spasm?

Dr. John A. Anderson, Salt Lake City, Utah: Dr. Toomey's comment about the change in the type of poliomyelitis which he has seen recently as compared to that which he saw many years ago I should like to support by relating briefly two rather serious epidemics that occurred in the state of Utah in the years 1943 and

1945. Four hundred cases occurred in 1943, about 10 per cent of which were of the bulbar or bulbospinal type.

The history of prodromes of a gastrointestinal nature was very frequent. However, in 1945, two years later, in the interim there being only 26 cases, there were again about 252 cases during the twelve month period, 46 per cent of the first 126 being the bulbar or bulbospinal type.

My colleagues and I do not know as yet whether we are dealing with a different virus antigenically, but certainly the nature of the clinical course of the disease and the onset were decidedly different in those two epidemics.

I should like to ask a question of Dr. Faber which may be of some interest. Does he think it possible that during gastrointestinal onset or prodromes the portal of entry is in the gastrointestinal tract primarily, or does the virus distribute itself through the circulation into the pharyngonasal and oral mucosa, thus having a portal of entry in which the clinical symptoms would initially be those of the bulbar or bulbospinal type?

Dr. Harold K. Faber, San Francisco: Dr. Toomey's question about the change in the character of the disease has been well answered by Dr. Anderson. My own impression is that epidemics do differ from each other to a limited extent in the distribution of the paralysis. The differences in severity, mortality and so on are usually ascribed to differences in the strain of the virus. Whether that explanation is true or not, I do not know. I do know that different strains of virus, as they are recovered in the laboratory, vary a great deal with respect to the ease of infection in the experimental animal and with respect to the extent of the lesions produced. We have seen strains which produce widespread lesions and relatively little paralysis, with a fairly high survival rate.

Dr. Toomey brought up a point in regard to control monkeys which I should have mentioned in the paper. We have studied control monkeys on a fairly large scale. We have separated them into two groups: (1) those animals which were killed soon after reception into the laboratory, and (2) those which had been in the laboratory for a considerable period of time. We reported on these about two years ago in the *Journal of Experimental Medicine*. We found that in monkeys which had been in the laboratory only a short time, less than two weeks, ganglionic lesions were very rare indeed. On the other hand, in monkeys which had been in the laboratory for some time we quite commonly found lesions in the peripheral ganglions. These data were obtained from cynomolgus monkeys, a species which is highly susceptible to poliomyelitis and which we believe to be nearer the human state of reactivity to virus than the more commonly used Rhesus monkey.

I was rather surprised at Dr. Toomey's comment on Drs. Harbits and Scheel's studies. My recollection of their case reports—and I have gone over the original paper several times—is that they report the finding of lesions in a reticular formation as well as in other parts of the brain stem in all of their cases. Howe and Bodian also noted the presence of lesions in the brain stem in all of their cases.

In regard to Dr. Smith's question about meningism, there is no question that there is a meningeal reaction in a fairly high percentage of cases of poliomyelitis. However, it is rather interesting to find in the series of 85 cases that I spoke of in the service of Dr. Brainerd in the San Francisco City and County Hospital, that about 10 per cent of the patients, including some examined as late as the eighth or ninth day of the acute phase, showed no changes in the spinal fluid at all.

In regard to Dr. Anderson's question of spread through the blood, I feel that that has been pretty well ruled out. A large number of studies of the blood to determine the presence of virus has been made. In a recent study at Yale, about 100 such examinations were made, in only 1 of which was there a positive result. As far as I know, the virus has never been detected in the blood stream in the preparalytic stage of the disease. I firmly believe that the disease is not spread through the blood stream, not only on the basis of tests which did not reveal the virus but also on the pathologic basis of irregular distribution of lesions.

Treatment of Hemophilus Influenzae Meningitis with Streptomycin. Dr. Hattie E. Alexander and Grace Leidy, New York; Geoffrey Rake, M.B., B.S., and Richard Donovick, Ph.D., New Brunswick, N. J.

Laboratory investigations were undertaken to explore the range of sensitivity in vitro and in vivo of a representative number of strains of Hemophilus influenzae, type B, and to devise a simple test which could serve as a guide to the therapeutic efficacy of streptomycin in a given patient with influenzal meningitis. The results are expressed in terms of the MEC (minimum effective concentration: the minimal concentration of streptomycin which when incorporated in Levinthal agar completely inhibits growth of an inoculum of 3,000,000 to 1,700,000,000 organisms after an incubation period of forty-eight hours) and of the MED (minimum effective dose: the smallest single dose of streptomycin which will protect 50 per cent or more of mice each of which has received 20,000,000 organisms [1,000,000 minimum lethal doses]). A high degree of sensitivity of this organism to streptomycin was demonstrated both in vitro and in vivo. The MEC of over 50 strains ranged between 0.8 to 10.8 units per cubic centimeter and the MED of 5 of these from 19 to

*Summary of Treatment of Twenty-Five patients**

Patients Treated, No.	Severity of Infection	Streptomycin Alone			Serum After 4 Days of Streptomycin			Streptomycin After Unsuccessful Use of Serum and Sulfonamide Compounds			Streptomycin, Serum, Sulfonamide Compounds Initially		
		R	S	D	R	S	D	R	S	D	R	S	D
13	Mild to average	12	..	..	..	..	..	1	..	..	..	..	..
8	Severe chronic	..	..	2	..	2	..	1	1	1	1	..	..
4	Severe early	..	..	..	1	..	..	..	..	..	3	..	..
					R			S		D			
Total					19			3		3			

* R indicates recovered; S, survived; D, died.

78 units per mouse. After exposure to streptomycin the strains in 2 patients exhibited resistance to more than 1,000 units per cubic centimeter. Likewise 16 sensitive strains subcultured in gradually increasing concentrations of streptomycin after a one to three week period thrived in concentrations exceeding 525 units per cubic centimeter. Results from mouse protection tests showed a high degree of correlation with those obtained in vitro. Whereas strains exhibiting a MEC between 0.8 and 10.8 units per cubic centimeter showed a MED of 19 to 78 units per mouse, those strains which resisted high concentrations in vitro proved to be equally resistant in mice. Doses as high as 5,000 units per mouse failed to protect 50 per cent of the mice.

Despite the agreement between the in vitro and in vivo tests, neither method enabled us to select in advance the patients whose strains became resistant after the beginning of streptomycin treatment. Our therapeutic results suggest that it is the severity of infection and therefore the size of the bacterial population which determines whether the strain from a given patient will become resistant.

While these procedures fail to detect traits of resistance in the original strains, their use in determining the sensitivity of organisms cultivated from patients after the start of treatment with streptomycin has provided a clear indication of the efficacy of this antibiotic for the patients from whom the strains were isolated. In the group of patients for whom streptomycin treatment proved successful all strains isolated from the spinal fluid or the respiratory tract after the beginning of the treatment were shown to be sensitive. On the other hand, treatment was unsuccessful for 2 patients whose strains exhibited strong resistance during administration of streptomycin.

The results of treatment of the 25 patients receiving streptomycin either alone or in conjunction with other agents are summarized in the table. The daily intramuscular dose was equivalent to 20,000 units per pound of body weight (44,000 units per kilogram). All the patients received daily intrathecal injections in quantities of 25,000 to 50,000 units.

Streptomycin represents an important contribution to the treatment of severe H. influenzae infections. The use of this agent alone was followed by prompt and complete recovery if the meningitis was of mild or average severity. In patients with severe infection, treatment with this antibiotic alone has been shown to have limitations. One of the causes for failures is emergence of resistance, which may be demonstrated soon after its occurrence by the use of the in vitro test described.

DISCUSSION

DR. JOHN A. TOOMEY, Cleveland: I feel that I can ask Dr. Alexander some questions that have occurred to me because I think that he really speaks with authority, ex cathedra, as it were.

Could Dr. Alexander tell the number of cases and the comparative results as regards partial and complete deafness between the two treatments, i. e., her old treatment and the new treatment with streptomycin alone? This is an embarrassing question for anybody, but I wondered if she had some explanation as to why the eighth nerve seems involved in these cases of meningitis—in any case of meningitis, for that matter. Why, for instance, isn't the seventh nerve involved?

Has she noticed whether streptomycin has done any harm when given intrathecally?

Finally, in comparison of her old method of treatment and the new, what were the mortality rates and the number of complications?

DR. GEOFFREY RAKE, New Brunswick, N. J.: I should like to say one word about deafness which occurs during treatment with streptomycin. Of course, it occurs not only in patients who have meningitis; in a recent survey of several hundred cases in which the patients have been treated with streptomycin, damage to the eighth nerve, with different symptoms and different degrees of symptomatology, has occurred in approximately 3 per cent.

Now, one of the questions has been whether the damage is due to streptomycin or to some impurity which is found with streptomycin, because of course the greater part of the streptomycin which is being used at the present time is not more than about 50 per cent pure. In connection with this problem, one group, studying the toxic reactions with crystalline streptomycin—I will not say "pure," but "crystalline"—has found that the same nerve damage can take place.

I say again not pure, because I much doubt whether the preparations of streptomycin which are being used in this particular study are much more than 95 per cent pure; therefore, it is conceivable, although not at all probable, that the damage to this particular nerve may still be due to some impurity which has been carried along with the streptomycin.

I should like to mention one further point. Dr. Alexander has mentioned that there is a certain amount of general truth in the statement that the different antibacterial substances which are used today have a tendency, when they are not used at the start in sufficiently high concentration, to bring out the resistant forms of the organisms by selection. Laboratory studies which are being carried on by my group, as well as by a great many other groups, are making it clear that this phenomenon is far more true of streptomycin than of the other common antibacterial substances with which we work today.

There is one very important practical reason for using combined therapy in these cases fairly promptly. In the first place, I believe that it is almost certain that the different substances, the sulfonamide compounds, the streptomycin and the serum, work at different points on the organism and therefore that these few resistant organisms which one has present when one starts to give the streptomycin can be taken care of by the sulfonamide compounds or by the serum. An important

practical point is that, as Dr. Alexander's studies have shown—and I really think I should say at this time that my name should not have been on this paper at all—in the 1 case to which she referred in some detail, the resistant strain has now persisted in the nasopharynx of the child for a long time, and if that happened too frequently there would be a large number of persons carrying these resistant strains which could set up meningitis insusceptible to treatment with this drug.

Dr. Horace L. Hodes, Baltimore: I should like to raise one question. Dr. Alexander subscribes to the theory that in any large population of organisms there are certain ones which are not resistant and are killed off and that the others, which are resistant, then take over, so to speak. However, in 1 case she started off with organisms presumably susceptible and at the end of twenty-four days had organisms which were resistant; then she said that the organisms became susceptible again. Does not that argue for the change of the organisms themselves rather than for the survival of members already resistant before treatment was begun?

Dr. John A. V. Davies, Boston: Several years ago it was my pleasure to comment on an equally excellent paper by Dr. Alexander in which she described the use of specific antiserum and sulfadiazine in the treatment of influenza type B meningitis. At that time, because of the confused state of evaluation of treatment and the multiple factors involved, my associates and I at the Children's Hospital in Boston attempted to simplify the treatment by using antiserum only. However, as a result of her experience and that of Dr. Downs in our laboratory, we bowed to Dr. Alexander and to fate, and have until recently treated H. influenzae meningitis with rabbit serum and sulfadiazine, with excellent results.

It has been our privilege only recently to use streptomycin, supplied to us two months ago. In this short time we have treated about 10 patients with streptomycin alone. This seemed to be a justifiable procedure for several reasons: In 8 of 10 cases the response shown by sterile cultures has been prompt. This response usually takes place within the first day or two. We felt that during this time we could give the patient the advantage of supportive measures, and soon determine whether or not bacteriologic response was taking place.

We have also hoped by using streptomycin alone to evaluate the clinical response, the recovery in relation to dosage, route of administration and length of time streptomycin is given, and possibly the relation of dosage to blood levels and levels in other body fluids.

It may well be that as a result of Dr. Alexander's experience and our own further experience we shall adopt the policy of administering antiserum also, posssibly to selected patients. Dr. Alexander has reminded us of the fact that H. influenzae may be resistant to streptomycin, or may develop resistance under treatment.

Dr. Hodes pointed out two or three years ago that H. influenzae type B is not a simple organism and that it is composed of several antigenic factors, related in some instances to type XXIX and type VI pneumococci; and it may not be beyond hope that we may in some way be able to recognize promptly which strains differ in respect to their ability or inclination to develop resistance to streptomycin.

Dr. Alexander did not mention one other point which may be important in our decision to use multiple therapy. As we snatch these desperately ill patients from death, as we prolong their lives, we may find that new situations develop which we did not see a few years ago. Complicating organisms for example may sometimes step in. We remember one child who apparently was doing well in recovering from H. influenzae meningitis when pneumococcus type 4 meningitis suddenly supervened. I know of 2 similar experiences in another hospital this winter, in which Staphylococcus aureus appeared to be the cause of death, in 1 case causing meningitis in a patient presumably recovering from H. influenzae meningitis.

Dr. Henry F. Helmholz, Rochester, Minn.: I was particularly interested in what Dr. Alexander said about the acquiring of immunity to streptomycin on the part of the influenza bacillus and merely wish to mention briefly some studies that my associates and I have made with organisms isolated from the urinary infection.

Exceptionally, an organism will have a considerable resistance to streptomycin. On the other hand, when one grows these organisms, colon bacillus, pseudomonas and other organisms found in the urine rapidly acquire immunity, so that a colon bacillus that will definitely be inhibited with from 30 to 50 units per cubic centimeter may within forty-eight hours grow definitely in a concentration of 1,000 units.

DR. HATTIE E. ALEXANDER, New York: In answer to Dr. Toomey's question on the incidence of eighth nerve deafness and other residual damage in patients treated with rabbit antiserum and sulfadiazine: Of the approximately 100 patients treated with antiserum and sulfadiazine, persistent cerebral damage occurred in only 1; numerous attacks of petit mal occurred. No examples of eighth nerve deafness were recognized. The follow-up period of the infant group is insufficient for evaluation of this point.

The meningeal infection of the patient treated with streptomycin who exhibited eighth nerve deafness was a mild one which cleared promptly. Administration of streptomycin was continued for three weeks because of the presence of the infection in three joints. While it is impossible to exclude meningitis as a cause, this causation is highly unlikely in the light of past experience. On the other hand, the type of lesion, involving both the cochlea and the vestibulum labyrinthi, is compatible with injury due either to meningitis or to streptomycin.

In answer to the question on the untoward reactions to the introduction of streptomycin intrathecally: Early preparations of streptomycin produced severe transient reactions in 2 young infants after intrathecal administration of 50,000 units. Since subsequent lots were well tolerated, the reactions were apparently due to impurities.

In answer to Dr. Hodes' suggestion that the resisant strain isolated after twenty-one days of treatment represented an example of adaptation as the result of influence of streptomycin on the organism: I must first make clear the fact that the organism isolated before therapy with streptomycin was found to be sensitive. Unfortunately strains isolated subsequently were not retested for sensitivity until twenty-one days had elapsed. The strains cultured from spinal fluid during this interval had already been discarded. We therefore have no information on the time necessary for the change in resistance. When large inoculums were used, a few colonies grew in the presence of 1,000 units per cubic centimeter. Subcultures in mediums free of streptomycin showed a rapid decrease in resistance; after several transfers the MEC was found to be 13 units per cubic centimeter. It was possible to confirm the resistance only by using a culture which had been dried and sealed under vacuum within five days of its isolation from the spinal fluid.

Following this experience we adopted the policy of determining sensitivity to streptomycin not only on original strains but on all strains cultivated after the beginning of treatment. We have detailed information on the other strain which exhibited resistance after the start of treatment. In that case, the strain isolated from spinal fluid withdrawn twenty-four hours after beginning the administration of streptomycin was resistant to 1,000 units per cubic centimeter. Colony counts on cultures grown in this concentration of streptomycin showed that 100 per cent of the population thrived. Subculturing in the absence of streptomycin at twenty-four or forty-eight hour intervals for a period of three months has failed to change the resistance of this strain. It seems clear that the degree of resistance of these two strains differs greatly. They may even represent two different mechanisms which bring about change in sensitivity to streptomycin. The resistance of the strain in which 100 per cent of the population thrived in 1,000 units per cubic centimeter has remained unchanged. This suggests that the resistant trait is a permanent one and that the sudden change in the sensitivity of the culture within twenty-four hours represents a selective process. All the sensitive members were killed within twenty-four hours, and the small fraction of members which could grow in the presence of 1,000 units per cubic centimeter proceeded to reproduce. It is

believed that these organisms represent mutants of the strain. There is reason to believe that all strains, if the population is large enough, contain mutants initially. In the patient whose strain was found to be resistant twenty-one days after the beginning of administration of streptomycin, only a part of the members were resistant, hence a large inoculum was necessary to demonstrate resistance. For some unknown reason the sensitive members overgrew the resistant ones.

Observations on the Therapeutic Effect of Desoxycorticosterone Acetate in Epilepsy. Dr. Irvine McQuarrie, Minneapolis.

In 1941, Dr. J. A. Anderson, Dr. M. R. Ziegler and I found the "convulsogenic" action of pitressin to be antagonized by the administration of desoxycorticosterone acetate in the case of a young man suffering from unusually severe grand mal epilepsy. The present communication is a report on the effects of the sterol on spontaneously occurring seizures in the same patient during the intervening five years. The sterol was administered at first in oil solution by daily intramuscular injections. Later it was given sublingually thrice daily in a propylene glycol solution. During the past two years it has been administered by subcutaneous implantation of 75 mg. pellets at intervals of about sixty days. Periodic examinations and frequent determination of the blood pressure and serum potassium have indicated successful avoidance of overdosage of the drug except for a short period at first when it was given intramuscularly in doses of 5 mg. twice daily.

The effect of the sterol as a sole form of therapy has been to reduce the number of convulsions from several daily to an average of one or two monthly. Periods of complete freedom from seizures have been as long as three months on several occasions. The interseizure electroencephalogram is normal except for very occasional spikes. One attempt in 1945 to discontinue implantation of the pellets resulted in the patient's going into a state bordering on status epilepticus for three months. During the past four months, bimonthly implantation of pellets has been supplemented by a small dose of phenobarbital (0.75 grain [0.045 Gm.]) once daily, with complete freedom from seizures.

Since the potassium content of the brains of normal rats treated continuously with the sterol was found to be reduced by 20 to 30 per cent without other important changes in composition, it appears likely that an alteration (in much smaller degree) in the potassium content of the brain cells constitutes a significant feature of the drug's anticonvulsive action.

Further studies are now in progress to determine the applicability of the method in other cases.

Growth-Stimulating Effects of Androgen. Dr. William C. Deamer, San Francisco.

Pituitary preparations to increase growth have proved disappointing to date. The most effective means of increasing height at the present time, in boys at any rate, is through the use of androgen-like substances, assuming that dwarfing due to hypothyroidism has been excluded. The close association of growth and sexual development is well known. Puberty is the most common example, but instances of adrenal hyperplasia or adenocarcinoma are also illustrative. In the latter the rapid growth which occurs early in the history of the patient is often arrested by premature closure of the epiphyses. This results in persons who, relative giants as children, become dwarfed adults. Any one using androgens to stimulate growth then must ask himself the question of whether his purpose may not be defeated by the rapid epiphysial closure such therapy may induce.

It was felt that the most suitable candidates for such therapy would be boys whose osseous age was retarded. Five such boys were chosen, all of them of very short stature and all having an osseous age three to seven years less than the chronologic age. Methyl testosterone was given daily over a period of six to sixteen months in the form of linguets which dissolved slowly in the mouth. The average daily dose varied from 3.5 mg. to 12.5 mg. The boys' ages varied from

8 to 14 years. The amount of growth in height obtained over that which was predicted for the 5 subjects individually was 80, 100, 300, 300 and 500 per cent. In other words, the poorest response was slightly less than twice the expected growth, whereas the best response was five times the expected growth for the period of therapy. The expected growth was calculated from data extending back from two and a half to six years before treatment. That a natural growth spurt due to puberty was not about to occur spontaneously was indicated by the osseous age, which in every instance was well below the range of puberty.

In 3 of the cases advance of osseous age during therapy was considerably more rapid than that of chronologic age, whereas in 2 the advance was the same as that of chronologic age. In no case, however, did the osseous age catch up with the chronologic age. It was felt, therefore, that we had not interfered unduly with opportunities for further growth.

For the present it appears that certain dwarfed boys whose osseous age is retarded may be suitable candidates for treatment with methyl testosterone sublingually as a means of inducing an increase in their rate of growth.

DISCUSSION

DR. DONOVAN J. MCCUNE, New York: I should like to ask Dr. Deamer whether he has had any experience in the use of testosterone in treating defective growth in girls as well as in boys. I tried it a few times and have found, as have others, that it will accelerate growth for at least a time. I have not pursued the trials long enough to know how long the effect endures.

One reflection occurs to me at this moment: This is that in the long search for a method of securing normal growth in stunted persons we have in the course of time come across a number of devices, to most of which reference has been made directly or indirectly during the course of these days' procedures: first, the use of growth-promoting preparations derived from the pituitary gland; second, as Dr. Talbot announced yesterday, alteration of diet; finally, as emphasized this evening, the administration of testosterone. I should like to be corrected if what I say is incorrect, but it seems to me that what has been proved by these measures is that growth can be accelerated in a good many cases but that in no case of which I am aware has the clinical aim, namely, normal stature in adult life, been reached. This is important in relation to the clinical use of these substances.

The mere knowledge that growth can be accelerated often leads the incautious clinician and the eager parent to expect more in the way of statural gain and social benefit than is warranted on the basis of what is at the present time chiefly a phenomenon.

DR. NATHAN B. TALBOT, Boston: In pursuance of these thoughts, it is interesting to consider the status of these children in the following fashion. If the osseous age is more retarded than the height age (ratio of osseous age to height age less than 1), then one has some leeway to work with. On the other hand, if the ratio of osseous age to height age is equal to or greater than 1, as was the case with many of the nutritional or so-called nutritional dwarfs whom we discussed yesterday, then it would not appear safe to rest satisfied with the observation that therapy with testosterone has not accelerated the osseous age beyond the normal for chronologic age. It is the relation of the osseous age to the height age which counts.

Second, if the drug is to be used, it may be worth giving intermittently, as one of Dr. Deamer's patients illustrated. Some of these children tend to keep on growing spontaneously after a short course of therapy, and spontaneous, normal growth is, of course, much more desirable than artificially induced growth.

DR. LAWSON WILKINS, Baltimore: My associates and I have been interested in this subject for some time. However, we have felt considerable hesitation in treating dwarfed children with androgens at an early age. We feel justified in treating patients who have reached 17 or 18 years and have remained sexually infantile because we assume that in all probability there was some deficiency of the pituitary gland that was going to keep them permanently infantile sexually.

In the absence of any effective growth factor of pituitary origin, we have felt that we could benefit these older subjects very much by developing their sex characteristics and by causing growth. As Dr. McCune pointed out, I am not sure that the ultimate increment of growth that is put on these children is any greater than they would ultimately acquire in the due course of years to come. On the other hand, when one encounters dwarfs or stunted children below the age of puberty or even during the adolescent years, one always pauses, hesitates and wonders whether one might not perhaps cause some harm in their endocrine system by substitution therapy and whether the administration of the sex hormones might not cause an inhibition of their own gonadotropic hormones and perhaps some permanent damage by inhibiting the development of their own gonads. Actually, I do not think that these small doses which are used for comparatively short periods of treatment do any harm, and perhaps one is justified in such treatment as has been described. On the other hand, I wish to urge a note of warning to the general medical profession against too liberal use of sex hormones in preadolescent children.

A few years ago physicians became fascinated with the idea that perhaps there were steroids chemically belonging in the group of androgens which might have a protein-anabolic and growth-promoting effect without any biologically virilizing effect. Dr. Fleischmann and I over a course of four or five years have had the privilege of examining a number of these androgenic substances with the hope that perhaps we would find some in that group showing strong protein-anabolic effect and little sex-stimulating effect. We have studied, I think, nine or ten such substances. Some of these have small nitrogen-retaining effect; others have apparently none. Studies of nitrogen balances have shown that the amount of nitrogen retention has in no case been at all comparable to that caused by the strong biologically virilizing androgens methyl testosterone and testosterone propionate. The results have been questionable in regard to whether they were really significant or not. We have treated boys for periods of four to six months with some of these questionable substances, such as 17-methyl androstenediol and 17-methyl androstanediol, and have been unable to demonstrate any significant growth effect or gain in weight. Some day such substances may be found. I do not think the search should be given up entirely. It is fascinating, but at the same time the results have been negative so far in finding any androgen that had these very desirable effects without having a strong virilizing effect.

Dr. William C. Deamer, San Francisco: In answer to Dr. McCune: We have not used testosterone for stimulation of growth in girls.

The notes of caution sounded by Dr. Talbot and Dr. Wilkins, I think, are in order, and we are in complete agreement with them. We do not think there is a wide field of usefulness for this type of stimulation of growth, but we believe it suitable in selected cases. We think that osseous age should receive particular attention, for sex hormones have also been used to arrest growth in tall persons by inducing epiphysial closure. That being the case, one is obviously on thin ice if sex hormones are used to influence growth uncritically.

All of our patients still have, even after testosterone therapy, an osseous age which is retarded. That gives us great comfort. It also indicates that these patients were not about to start a natural puberty growth spurt, as in each case the osseous age was below the usual age of puberty.

We recognize the fact that we may be just borrowing future height and may not really be making these persons any taller than they ultimately would have been anyway, but we do give them that height at a time when it is extremely important to them. I need not explain to this audience that there is a factor of morale that is important.

One of these boys came to us in connection with his application for a home teacher. He was ready for high school and had an intelligence quotient of 110 but was so conscious of his short stature that he did not want to go to school. The use of androgen was an important factor in assisting his subsequent good adjustment at school. He was one in whom the increased aggressiveness that

resulted was of value. Instead of having his mother struggle for a place on a crowded street car for him, he now fights his own battles. More of value has happened to him than just an increase in height.

Some Epidemiologic Studies in Dental Caries. Dr. Julian D. Boyd, Iowa City.

As a background for controlled studies relating to the prevention of tooth decay, the pattern of dental caries in various groups of Iowa children has been studied and the results subjected to statistical analysis. The findings have emphasized the multiplicity of factors which may be expected to modify the incidence of caries both in individual subjects and in contrasted populations of children.

The serial course of caries in the teeth of 100 presumably healthy children over periods of years has demonstrated that caries progressed almost without exception, even though these children were under recurrent dental care of an acceptable standard. Such care, even though it did not prevent or possibly did not lessen the rate of development of new carious lesions, did serve to preserve the teeth from need for extraction. Great individual variation was noted in the rates of progression of caries, not only from subject to subject but also in the same child at successive periods of observation.

When the rates of carious advance in these presumably healthy children were compared with those observed in groups of children with various specific chronic diseases or deformities, notable group variation was evident. In children under treatment for hereditary syphilis or for correction of orthopedic deformities, further caries developed at about half the rate of the normal group; in diabetic children the rate was about one-tenth that of the normal, whereas among children with rheumatic conditions the rate was greater than among the normal subjects.

The control group of children lived in an area where domestic water supplies were essentially free from fluorides. To determine the pattern of caries in relation to ingestion of fluorides surveys were made in three state custodial institutions and among the high school population from an area of endemic fluorosis. When separate consideration was given to those children with and without mottling of enamel respectively, regardless of their current residence, the incidence and extent of caries were found to be about three-fourths as great among those with mottling as among the others. However, of the children without mottling, the incidence of caries was no less among those living in an area of presumably therapeutic level of fluorine supply than among those from the institutions, in which the water was essentially fluorine free.

These studies are still in progress; they represent part of a long range program. The results thus far obtained illustrate the need for great care in the conduct of studies in the field of prevention of caries and for caution in the acceptance of published reports on this subject in which adequate controls were not established. The advantage of long term studies of individual subjects over cross-sectional studies of large populations is emphasized.

The Uncovered Child. Dr. Charles Hendee Smith, New York and New Brunswick, N. J.

The problem of keeping the infant covered begins in the earliest days of life. A visit to almost any obstetric nursery will find more than half of the infants lying with bare arms and legs. According to the usual nursing technic, the blanket is merely folded over the baby, who promptly throws it off by his active motions. Fortunately, the newly born infant is relatively immune to infections of the respiratory tract, but this immunity is soon lost; after a few weeks the baby who gets uncovered at night, or during daytime naps, begins to have colds from the resultant chilling. The problem of recurrent or persistent colds looms large in active pediatric practice. Careful histories show that the correlation between these colds and getting uncovered during sleep is extremely high. When

proper methods of keeping the child covered are instituted, the response to treatment of infections of the respiratory tract is usually accelerated.

The baby is not the only one to whom this matter is of importance. The mother gets up again and again during the night to replace the bedding, and her loss of sleep and resultant fatigue lower her resistance so that she catches the baby's cold, or gives it to him if she is the first victim. The father seldom escapes, for his rest is disturbed, and he usually shares the family infection.

The reaction of most mothers to this problem is the same. They regularly try to keep the baby warm by putting on more or heavier night clothes. The "sleeper" made of heavy cotton flannel seems the easiest solution, for it is sold in all baby outfit stores and is widely advertised as the method of choice for keeping the child warm when he crawls out. Under this garment, which is the equivalent of heavy pajamas with feet, the baby usually wears a heavy undershirt, often double breasted, in addition to the diaper and diaper cover. Clothed in this way, he soon becomes too hot, and he will struggle out from under the bedding, if he is physically able to do so and not feebleminded!

The experience of mankind in all countries and climates has taught that the way to keep warm in bed is to wear little in the way of night clothing and to use enough bedding to prevent radiation of the body heat. One has only to think of the subjective sensation of trying to sleep in two heavy shirts and long heavy drawers and socks to realize the absurdity of trying to keep an infant covered under equivalent conditions. When a mother is asked whether she could sleep wearing this amount of clothing the answer is invariably a laugh and an emphatic "No!"

The young infant is easily kept covered by means of a simple sleeping bag. A "receiving blanket" folded to lap 4 inches (10 cm.) and sewed up across the shoulder and, leaving 4 inches open for the neck, serves the purpose well. In summer it may be made of sheeting. Under this bag the baby wears a light shirt and a diaper and diaper cover, but no nightgown or pajamas. The infant may be kept in it day and night to the age when he begins to use his hands and at night or nap time until he approaches a year. The use of the bag often conditions him to stay covered during sleep, so that he makes no attempt to get uncovered, unless the mother puts on too many clothes.

As soon as the baby is old enough and strong enough to attempt to get out of the bag, its use should be abandoned. But some means of restraint is more needed than ever, for it is in the babies from about 8 to 24 months old that infection of the respiratory tract is most frequent and serious. For this age the manufacturers of baby wear offer nothing but the sleeper or thin pajamas. For several years we have taught mothers to make a nightgown, using the top of the sleeper to save trouble in fitting sleeves and to it sewing a skirt of any available material. To the back of the skirt a strong band of doubled and stitched cloth is sewed vertically, extending about 12 inches (30 cm.) below the bottom of the skirt. This amounts to a strong tail to the garment, which can be tied to the foot of the bed or to another such band fastened to the springs and coming up over the foot of the mattress. The child is thus prevented from crawling toward the head of the bed. If the blankets are wide enough to tuck in well and are fastened to the crib rods by taking a loop around them and using a strong safety pin or blanket clips, the child cannot throw off the bedding. He can turn over freely and move from side to side, but he cannot get uncovered. He soon learns to settle down to sleep when he is tucked in. The mother can also go to sleep with a clear conscience, knowing that she will find her baby under the covers in the morning.

The large "snuggle" bags on the market are usually too heavy, too strong around the neck and not without the danger of choking the baby. The harness around the chest with bands or tapes fastened to the bed is a very dangerous contrivance. I have known of 2 fatalities caused by the strangling of the baby with the tapes.

Penicillin in the Treatment of Diphtheria and the Diphtheria Carrier State. Dr. Samuel Karelitz, Dr. Lewis R. Wasserman and Dr. Ralph E. Moloshok, New York; Dr. Cyrus W. Strickler, Atlanta; Dr. Edwin J. Adamski, Chicago; Dr. Jacob Light, Baltimore, and Dr. Charles Hoffman.

Eighty patients with faucial diphtheria, 61 among German prisoners of war and 19 among American soldiers overseas, were treated with antitoxin and penicillin. These patients were seen in five United States Army hospitals in one of the European base sectors. The dosage of penicillin was 20,000 units every three hours in 53 cases; 20,000 units every two hours in 21 cases, and 25,000 units injected intramuscularly every three hours in 6 cases. The results were favorable and similar in all groups.

Comparing the composite data with observations in 42 control cases and with data in 457 cases observed by Hartley and Martin, a significant reduction in the time during which cultures of material from the nose and throat yielded Corynebacterium diphtheriae was noted in cases in which penicillin was administered, the organism having disappeared in 92.5 per cent within ten days, as compared with 7.8 per cent in our control cases and 35 per cent in the cases reported by Hartley and Martin.

Spraying the nose and throat with a saline solution of 1,000 units of penicillin per cubic centimeter hourly during the day and every three hours during the night for seven days resulted in disappearance of the organism from the throat cultures of only 2 out of 21 patients with faucial diphtheria.

The same local penicillin treatment of carriers continued for seven days met with favorable results in 8 cases in one hospital but failed in all but 2 of 13 cases in another hospital when the treatment was continued from seven to twenty-three days. Penicillin given intramuscularly to convalescent carriers in a dosage of 20,000 units every three hours resulted in cessation of the carrier state in 10 of 14 cases within a period of four days.

It is stressed that administration of penicillin must be continued until three daily cultures which fail to yield the organism are obtained and must be resumed promptly if C. diphtheriae reappears soon after the treatment is stopped.

Data from the literature are cited which indicate that most strains of C. diphtheriae are inhibited by concentrations from 0.25 to 1.0 units of penicillin per cubic centimeter. To attain such concentrations in the blood it is suggested that larger doses of penicillin, possibly 30,000 or 40,000 units and even larger amounts given intramuscularly every three hours, may be needed.

Complications such as cervical adenitis or otitis media are eliminated by therapy with penicillin, if the complication is present before treatment is started, and prevented thereafter during the course of the disease. On the other hand, complications due to diphtheria toxin occurred in 2 of the 42 control patients and in 7 of the 80 patients treated with penicillin and seemed unaffected by penicillin.

It is emphasized that penicillin should not be given without antitoxin in cases of acute diphtheria but should be used only together with diphtheria antitoxin.

DISCUSSION

Dr. A. Ashley Weech, Cincinnati: I wish to say a few words in support of the conclusions which Dr. Karelitz has drawn. During the past year I have seen a number of patients with undiagnosed diphtheria who had been treated with penicillin prior to entry into the hospital. Although a few patients handled in this manner may possibly have been improved or even cured, it is natural that I should see only those who were brought to the hospital after treatment had failed. It seemed clear that penicillin was not the method to be chosen in the management of diphtheria. Indeed, I believe that steps should be taken to reeducate a medical public in the diagnosis of diphtheria and to attempt to bring a realization that penicillin is not a cure for all infections.

DR. HORACE L. HODES, Baltimore: My associates and I in Baltimore are in a much worse position than Dr. Weech. Since Jan. 1, 1946, at Sydenham Hospital, where nearly all patients with diphtheria in Baltimore are treated, we have had about 200 children and adults with diphtheria since January.

It seems clear that the use of penicillin has not made any great difference in the treatment of diphtheria. Our mortality is about 6 per cent, just about what it has been for years.

I should like to say one thing about the carrier problem. The diligence with which one looks for diphtheria organisms in the throats of these children, and of adults too, determines to a large extent the carrier rate. For instance, we use three different culture mediums, and we often find, for example, on Pai's mediums that we will have a positive result, whereas on the egg mediums the culture may fail to yield the organism. The next time it is done, the reverse may be true. Also, a great deal depends on the manner in which the culture is taken, when it is taken, how the throat is irrigated and who takes the culture. We have many times again obtained the organism from children whose cultures have failed to grow it on all three mediums for three, four and five days. In the evaluation of any agent used as a means of reducing carrier status, these points must be taken into consideration. My own experience with the use of penicillin is that it has been disappointing in the control of the carrier state.

Finally, most of the children with diphtheria whom we see have been inoculated against diphtheria at some time. The majority of them have been inoculated longer than three years before. We think that unless a child is inoculated at 6 and 7 months, again at 3 years and again at 5½ or 6 years, at least in Baltimore, he is running a substantial risk of contracting diphtheria.

DR. HARRY H. GORDON, New York: The previous speakers have called attention to some factors responsible for an increase in diphtheria. I should like to point out another factor, the occurrence of diphtheria bacilli in cutaneous ulcers of returning soldiers, particularly those from the Pacific areas.

As you know, there was a good deal of concern about the introduction of tropical diseases into this country by returning soldiers. It has become obvious that much of our concern was unwarranted. In the case of malaria, because of prompt treatment of previous attacks, it is unusual to find an American soldier carrying gametocytes in his blood without symptoms which would call attention to the need for treatment. In the case of filariasis, few soldiers have had microfilarias in their blood, and therefore they cannot be a source of infection for mosquitoes. In schistosomiasis, although the soldier may be passing ova in his stool without symptoms, so far as is known no American snails will transmit the disease.

In the case of diphtheria, however, the situation is different. In the first place, no intermediate vector is necessary for transmission. Second, virulent diphtheria bacilli have been found in cutaneous ulcers, some of which may be recognized clinically as cutaneous diphtheria. Organisms have also been found in lesions that are not characteristic and in the noses and throats of patients with other cutaneous lesions.

Col. Francis Dieuaide, on the basis of findings in the South Pacific, called to our attention at the Harmon General Hospital the need of watching for diphtheria. A careful survey was initiated by Col. Worth Daniels and Major Eric Denhoff of all patients admitted to the hospital. It was found that some 5 per cent of patients admitted to our dermatologic wards were carrying virulent diphtheria bacilli in either nose or throat or in open cutaneous lesions. In patients admitted to general medical wards from the South Pacific, the incidence was virtually nil, and in patients admitted from the European theater, again the incidence was virtually nil. We have, then, in patients with chronic dermatitis contracted in the Pacific or in patients who have been in contact with them a group of people who may be carrying virulent diphtheria bacilli and who may be, in some instances, the sources for the increased infections that Dr. Weech and Dr. Hodes have mentioned.

DR. BELA SCHICK, New York: The presence of diphtheria bacilli has a great importance in the problem of immunization. Dr. Karelitz has pointed out that the incidence of carriers is higher in persons in congested quarters—such as soldiers in barracks and persons in overcrowded districts of large cities. About 1923, 2 per cent of the population of New York city were found to be carriers, many of them immune to diphtheria. These persons are responsible for silent immunization.

The presence of diphtheria antitoxin showed a regular curve according to age. Eighty-five per cent of adults and newborn children were immune to diphtheria. The question whether a person is a carrier or not is important for members of professions who have contact with children, such as teachers, nurses and physicians.

The frequency of finding antitoxin in the serum of children admitted to the wards of the hospital makes these children relatively innocuous for the other children in the ward even if they are carriers of diphtheria bacilli. All children admitted to the ward are given the Schick test. Susceptible children are thus known. I have abandoned, therefore, the practice of making cultures for diphtheria bacilli on a patient's admission.

The widespread active immunization against diphtheria did away with many cases of active disease. This may have an influence on the frequency of carriers. Therefore, a change is to be expected through the development of silent immunization. This may change the age distribution of immune persons.

Cutaneous diphtheria is an important diagnosis. It is frequently overlooked. It is impressive how quickly such a condition clears up if it is treated with antitoxin.

DR. JOSEPH STOKES JR., Philadelphia: I was also interested in the question of cutaneous diphtheria and its relationship to faucial diphtheria and was wondering about the possible relationship in Dr. Karelitz' experience.

Another question that came up in several of the war theaters was the relation between symmetric motor disturbances, a high content of protein in the spinal fluid and a low cell count. Many of the British physicians in the Mediterranean theater felt that this relationship was due to diphtheria.

I was wondering what Dr. Karelitz' experience had been in that field. The study is extremely interesting, particularly because of the difficulties of carrying it out in a war theater.

DR. SAMUEL KARELITZ, New York: Thank you, Dr. Weech, for reenforcing that warning. I will repeat it: Penicillin should not be used without antitoxin in acute diphtheria.

I was aware of your failure to get results in Baltimore, Dr. Hodes. I have no explanation for it except to suggest the possibility for the need of larger doses used for a longer time.

In regard to Dr. Smith's experience, I gained the impression that after a reversion when the organism was again obtained by culture, she did not reinstitute therapy with penicillin. Had that been the case with us, we too should have reported more failures. We had patients in whom the culture failed to yield the organism after the first twenty-four or fifty-eight hours of treatment with penicillin. Cessation of treatment was followed by a reversal with positive cultures in one to five days. If we did not reinstitute treatment of such patients immediately, we had difficulty.

In one hospital where 46 patients with diphtheria were followed, those in charge gave only 20,000 units of penicillin every three hours for three days to one group, and to another group 20,000 units every three hours for five days. Cultures were taken before the beginning of treatment and two weeks later. Two weeks after admission the organism was obtained from more than 50 per cent of those that were treated for three days and from about 25 per cent of those that were treated for five days. Many of these patients were transferred to another hospital, where penicillin was again administered. In many of the cases the infection was difficult to clear up. We had the impression that some of those

strains of C. diphtheriae had developed resistance to penicillin. We were unable because of limited facilities to confirm this impression in the laboratory.

Dr. Gordon's remarks were interesting, and I think that again shows the difference in diseases in different parts of the world. I should like to take this opportunity to answer Dr. Stokes's question simultaneously. We looked for cutaneous diphtheria especially in cases of tropical ulcers but rarely found it. We had some cases of wound diphtheria. Some patients had faucial diphtheria first and later infected their wounds. On the other hand, there were patients for whom cultures of material from the throat did not yield the organism, and it was present only in material from the wounds. Treating these patients with penicillin locally was not successful. We were just starting intramuscular administration of penicillin for the wound diphtheria when the officer treating the patients was transferred and the use of penicillin was discontinued for patients with diphtheria in that hospital.

I should like to comment a bit further on both Dr. Gordon's and Dr. Schick's remarks. When diphtheria broke out in Sicily, some of the contacts were transferred to our hospital in Africa. A small outbreak of diphtheria occurred in one of our surgical wards. One of our ward attendants and 1 of our nurses acquired diphtheria; hence we decided to give every one in the hospital at the time, about 1,300, the Schick test. I was amazed to find results of 35 per cent of the Schick tests positive among those who had not previously been immunized, because I had been led to believe the usual incidence was about half that, or less. Among the nurses and physicians who were tested, 25 per cent of the results were positive. We were able to reverse the results of the Schick test in many of the physicians and nurses with small doses of toxoid, one or two doses of 0.2 cc. of toxoid after the Maloney skin test. I should like to warn against the use of large doses of toxoid among adults without testing the patient for sensitivity, because in adults there are pretty severe local and general reactions from the ordinary clear toxoid.

Dr. Stokes, I am glad that you asked a question about changes in the spinal fluid. Such changes first came to our attention when a soldier with wound diphtheria had a spinal fluid protein content of 165 mg. per hundred cubic centimeters but no increase in cell count. This man apparently had wound diphtheria for many weeks, and increase of protein in the spinal fluid persisted for nearly three months. In several of the hospitals in Tunisia and Southern Italy patients appeared whose illness had started with membranous tonsillitis, but from whom C. diphtheriae could not be cultured. These patients later presented cranial nerve palsies, and elevation of spinal fluid protein without an increase in cells. Although they were regarded as having the Guillain-Barré syndrome, we questioned whether some were not suffering from late effects of diphtheria.

These experiences prompted us to do lumbar punctures in cases of faucial diphtheria with and without neurologic complications. I do not remember the exact number, but I believe that examination was made of the spinal fluid of 8 or 9 patients without neurologic complications. One had a protein of 62 mg. per hundred cubic centimeters, which was a definite elevation according to the normal figures we were getting from the laboratory.

There were about 12 patients with toxic neurologic changes, of whom all but 2 or 3 had some elevation of spinal fluid protein. The figures ranged from a total of 50 mg. to about 135 mg. per hundred cubic centimeters, if I remember correctly.

I was unaware of this finding before, but I later learned that it was well known that an increased content of spinal fluid protein occurred in cases of neurologic complications of diphtheria.

Epidemiology of Streptococcic Infections. Dr. Francis F. Schwentker, Dr. Horace L. Hodes, Dr. John L. Peck Jr., and Dr. Beach Chenoweth, Baltimore.

Strains of streptococci differ epidemiologically from each other in at least two ways: their ability to disseminate themselves among the population and thus cause

disease and their ability to produce scarlet fever. The latter characteristic may be entirely independent of the other disease-producing abilities. The disseminative ability of a particular strain is apparently an intrinsic characteristic of the strain and is independent of other organisms and of the environment. Carriers are, in effect, resistant or immune persons who have become infected with the organism.

DISCUSSION

DR. JOSEPH STOKES JR., Philadelphia: I wish to ask Dr. Schwentker a question. In Philadelphia during the early stages of the development of Bainbridge, a large series of cases of glomerular nephritis were encountered. I was wondering whether Dr. Schwentker has seen any relationship between the type of organism found at Bainbridge and the peak, apparently, of glomerular nephritis that occurred.

DR. FRANCIS F. SCHWENTKER, Baltimore: The patients with streptococcic infection were in general moved to the hospital, which was really a separate part. It was not until later that we got to work over there, and there were not enough data at the time I left to be able to correlate the type of disease with the complications that occurred. Dr. Hodes stayed for almost a year after I left Bainbridge. He may be able to answer this question.

DR. HORACE L. HODES, Baltimore: In answer to Dr. Stokes's question, there was no specific relationship of any one type of streptococci to the occurrence of nephritis and rheumatic fever. Type 6 caused most of the streptococcic disease in general and was associated with most of the nephritis and rheumatic fever. However, we encountered nephritis and rheumatic fever among persons who had experienced infection with one or more of the other three or four types which were widely distributed among persons at the station.

Parenteral Fluid Therapy in Diarrheal Disease. DR. A. M. BUTLER, DR. N. B. TALBOT, DR. J. D. CRAWFORD, DR. E. A. MACLACHLAN and DR. J. APPLETON, Boston.

Because it has been shown in acute nutritional disturbances in infants, in diabetic acidosis and in dehydration due to thirsting that the ratio of loss of potassium to loss of nitrogen exceeds the ratio which pertains in normal tissue; because some experiments which we have conducted on the rehydration of dehydrated subjects have indicated that much of the water and sodium of the parenterally administered repair solutions of dextrose and sodium chloride may go into tissue at the expense of repair of extracellular fluid, and because of Darrow's important contribution to the role and use of potassium in hydration therapy, we have attempted to obtain descriptive data defining the physiologic needs in dehydrated infants and their utilization of substances administered therapeutically.

The descriptive data pertaining to the need and utilization of water, sodium, chloride, potassium, nitrogen and dextrose obtained from balance studies on such patients are shown graphically on seven slides. These slides illustrate particularly: (1) the excessive loss of potassium as compared with nitrogen in the course of dehydration due to diabetic acidosis; (2) the repair predominantly of intracellular fluid which may occur with the provision of dextrose solution alone or of dextrose in one-half isotonic solution of sodium chloride, and (3) the response of three diarrheal infants to the parenteral administration of the substances just enumerated.

On the basis of such information, we have adopted a basic solution for parenteral fluid therapy in dehydrated subjects which contains 2.24 Gm. of sodium lactate, 0.58 Gm. of sodium chloride, 0.89 Gm. of potassium chloride and 0.25 Gm. of potassium monohydrogen orthophosphate per liter of 10 per cent dextrose solution. In terms of milliequivalents this solution contains 30 milliequivalents of sodium, 22 milliequivalents of chlorine, 15 milliequivalents of potassium and 3 milliequivalents of hydrogen phosphate per liter. After infusing fairly rapidly about 15 cc. per kilogram of half-isotonic solution of sodium chloride in 5 per cent dextrose solution per kilogram in order to improve the circulation and renal

function, this potassium-containing solution is injected parenterally at the rate of 0.8 cc. per minute in small infants and 4 cc. per minute in adults. In infants the total amount per day varies from 200 to 150 cc. per kilogram, the amount being inversely proportional to the size of the infant. In adults the total amount per day approximates 4,000 to 6,000 cc. We have used such parenteral fluid therapy in the treatment of some 30 dehydrated infants and 2 older patients with diabetic acidosis. No elevation of serum potassium or change in the electrocardiogram has been observed. This potassium solution was administered to a small infant for one hour at the rate of 2.5 cc. per minute and to an adult for one hour at 8 cc. per minute without significant rise in serum potassium or change in the electrocardiogram.

Intravenous Alimentation of Infants for Extended Periods. Dr. Katharine Dodd and Dr. Samuel Rapoport, Cincinnati.

It is shown that maintenance of fluid and electrolye equilibrium by administration of parenteral fluids is possible even in small infants during periods of partial or total withdrawal of oral feeding. With the use of dextrose, whole blood and plasma, and casein hydrolysates, a gain in weight may be achieved during the period of parenteral feeding.

A daily record of total intake of fluid, saline solution, calories and nitrogen as part of a careful plan is essential in such a program.

Frequent observation of the clinical appearance of the infant and of his electrolyte and osmotic equilibrium is necessary.

Wide variation may be permitted in total fluid intake provided the intake of sodium chloride is carefully regulated and is not excessive.

Premature and young infants have a low saline requirement.

Contamination of the fluids given, infection at the site of needle punctures and thrombosis of the veins present a considerable problem. By the use of a closed system of administering fluid and the addition of penicillin and merthiolate to the solution of casein hydrolysate, the more serious difficulties have been almost completely overcome. Thrombophlebitis and wound infection continue to be troublesome.

DISCUSSION

Dr. Donovan J. McCune, New York: Dr. Butler's renovating solution is evidently designed for mass application; that is, it contemplates the average situation which may be expected to respond to this solution administered according to the regimen which he described. It occurred to me to wonder how commonly he has encountered pathologic situations which are so far from the average that the solution is not appropriate in exactly the amounts which he suggested.

Second, does he consider it desirable to identify such situations by chemical means in advance and to follow their progress, and hence the appropriateness of therapy, during its course?

Dr. A. Ashley Weech, Cincinnati: My unique position in Cincinnati has brought me the privilege of watching first with interest and then with growing enthusiasm the work which Dr. Dodd and Dr. Rapoport have been doing in the management of these babies with disturbances which require parenteral therapy.

The charts that Dr. Dodd has presented speak for themselves. One does not need to stress the fact that one sees very ill babies in Cincinnati with this type of disease, and that some of them have recovered has astonished all concerned.

If I were to pick out one point to stress, it would be the value in the wards of the fluid summary sheet which permits keeping track of a planned system of therapy. More than a year ago my associates and I were confronted with a sudden outbreak of diarrhea of the newborn in a neighboring hospital. On one Sunday afternoon 10 infants were admitted with severe diarrhea. Although our residents knew how to calculate the requirements of these infants, the system broke down when two residents had to make the calculations separately for 10 different infants. It became plain that a system was essential which would permit the

entry of a few simple figures and a rapid approximation of what the needs of each baby would be.

I might add that not very long ago one of our residents, Dr. Carl Weihl, summarized the approximately 280 cases of diarrhea in which there had been treatment in our division during the period following the interest exhibited by Dr. Dodd and Dr. Rapoport. We were all surprised at the result because the babies that do badly have a way of lingering in memory and those that get well are forgotten. The fatality rate in this group was 5.7 per cent, which contrasts with a figure of 35 to 40 per cent several years earlier. This planned system of attack with a careful keeping of records can definitely be said to yield a rewarding result.

DR. EDWARD M. BRIDGE, Buffalo: Dr. Butler's paper and the several others dealing with potassium at these sessions have stimulated us all to think in terms of potassium needs.

I would like to call attention to one fact which was presented about fifteen years ago by Dr. Bengt Hamilton of this Society, which suggested that changes in potassium-sodium balances might apply to conditions other than replacement of fluid. Most of the reports of these last few days have been related to dehydration or starvation. Dr. Hamilton was impressed with the fact that every now and then a child might be given a large infusion of a saline solution and instead of excreting it might retain it all. He therefore placed several children on a metabolism frame, gave them about 500 cc. of a saline solution subcutaneously and followed their balances of sodium, potassium, nitrogen, phosphate and other substances for about ten days. He was fortunate in having 1 child who retained the entire 500 cc. as gain in weight. In the course of the following ten days the sodium was gradually excreted and the potassium was correspondingly retained.

I suspect that in the process of growth there may be a shift between extracellular and intracellular fluid which may enter into the problems of recovery from dehydration as well.

DR. SAMUEL RAPOPORT, Cincinnati: As one whose interest has been primarily chemical, I should like to stress the tremendous chemical interest that is derived from a close, continued and cross-sectional attempt to study as many babies as possible. Unfortunately, I do not have slides illustrating all the unexpected changes that we have observed in the past few years in the ward. We have observed babies with diarrhea whose total concentration of electrolytes was only 115 milliequivalents per liter. Not all of them have been acidotic. As a matter of fact, patients with some of the most severe dysenteries are apt to be admitted with a normal bicarbonate content and a normal p_H. On the other hand, some babies, particularly those with a history of high fever and insufficient intake of fluids, have come with hyperelectrolytemia to the extent of 190 milliequivalents, which raised the osmotic concentration of their plasma into the neighborhood of 450 milliosmols per liter compared with the normal value of 310.

I should like to stress the point that each of the premature babies that were shown had a sodium concentration of 160 to 170 milliequivalents per liter during the period of acidosis.

From this diversity there is, I think, one conclusion of clinical importance, and that is that no single solution will be suitable for treating all babies, particularly because all those babies, whether in shock or not (shock is a flexible term, a term that one can do well without in describing the condition of these babies), have some type of renal dysfunction. All of them present the problem of inability of dealing with administered electrolyte. Therefore, we have kept the salt intake at a minimum. To normal subjects large amounts of salt may be given without concern, but by these babies salt is handled with difficulty, and only close chemical checking can insure one that in the effort to maintain the salt balance one does not trespass beyond the danger line. We have done that. We have occasionally given too little salt when we have not checked closely enough with deleterious results.

DR. GEORGE M. GUEST, Cincinnati: Dr. Butler referred to the losses of potassium and of nitrogen from the body that occur during periods of acute dehydration and acidosis, calling attention to the fact that the loss of potassium during the development of acidosis is far greater than would be expected if the potassium and nitrogen were coming from the breakdown of whole tissue cells or proteins; also, that the retention of potassium during periods of recovery is greater than would be expected from the measured nitrogen retention. It should be emphasized that this is especially true in conditions of rapidly developing acidosis when catabolism of labile intracellular constituents occurs without, necessarily, a breakdown of whole cells. In conditions of starvation or of disease involving destruction of tissues, the losses of potassium and nitrogen from the body would be proportional to that expected from the breakdown of whole cells. It should be borne in mind that the restoration of whole tissue cells and proteins may require many days or weeks, whereas the labile constituents of the cells when reduced during acute metabolic disturbances can be restored quickly, within a few hours. Parenteral fluid therapy employed in acute disturbances is directed primarily to the replacement of labile constituents. I have already mentioned here certain similarities between intracellular metabolic reactions in the red blood cells and in other tissues of the body. Changes of labile intracellular stores of potassium and phosphorus can be measured most easily in erythrocytes: for example, during the development of diabetic acidosis there is a sharp reduction in the concentration of potassium and of organic phosphates in the blood cells, and during recovery the concentrations of potassium and phosphates in the cells show parallel increases to normal. In vitro, movements of potassium and phosphorus out of and into intact erythrocytes are easily demonstrable under changing conditions that affect the reactions of the glycolytic enzyme system by which the labile organic phosphates are broken down or synthesized. In incubated blood, when the sugar is exhausted by glycolysis or the p_H is lowered, inorganic phosphorus and potassium rapidly escape from the cells, but both will be taken up again by the intact cells if sugar is added and the p_H is adjusted to an optimal range. One can justifiably assume that similar rapid shifts of intracellular potassium and phosphorus take place in vivo under conditions of acidosis and recovery.

These comments are offered in support of Dr. Butler's use of both potassium and phosphates in the formula he has employed for parenteral fluid therapy. There is a great need for more information by which conditions under which such therapy is best employed can be defined and by which quantitative requirements can be predicted.

DR. ALLAN M. BUTLER, Boston: The rate of administration of these potassium-containing solutions is 0.8 cc. per minute for an infant and up to 4 cc. per minute for an adult.

I of course agree with Dr. Dodd that if a patient continues to lose fluid during the course of parenteral repair of dehydration and provision of maintenance needs one must take into account the amount of fluid and electrolyte so lost and make provision for the repair of such losses in the administration of parenteral therapy. Otherwise it will be noted, as Dr. Dodd remarked, that the patients always remain underhydrated.

My co-workers and I also have encountered, within the last few weeks, a severe type of infectious diarrhea of the newborn. A number have arrived in our hospital from several hospitals in Boston. The diarrhea is the most pernicious I have ever encountered, and it is obviously like Dr. Dodd's. We have maintained patients on therapy with parenteral fluids, with very little fluid given orally, for from ten to sixty-two days, with apparent recovery of even one that received parenteral fluid for sixty-two days. We have had about 23 of these patients. One has died as a result of aspirating some diluted milk that was being given at night as oral feeding.

The importance of plasma and whole blood and of amino acids in such patients for whom long-continued therapy with parenteral fluids is required of course ought to be stressed. The patients need such supportive therapy.

Dr. McCune raises the question of whether an average solution can be used to treat all these babies. Dr. Rapoport has given figures presenting the extremes in the concentration of electrolytes in patients as they turn up for such treatment. I agree with him entirely. One has patients who when seen have a serum sodium content as low as 115 or as high as 180 mg. per liter. Should a single parenteral fluid be used for the correction of the disturbances in those patients? I think it should not, but I think one should start with a routine procedure, and then ask the laboratory to make a few relatively simple determinations which will orient one as to what type of patient is being dealt with, whether a child with relatively little disturbance in concentration of electrolytes or one with definite dilution or definite concentration.

The analyses one needs are of serum sodium, serum chloride, serum protein and hemoglobin. If one wishes to include an analysis of serum carbon dioxide this may be done, but I do not think such an analysis is half as important as the four analyses mentioned, because one can give a solution which is almost foolproof in correcting the acidosis or alkalosis. Also, the patient's history will indicate to a considerable extent which condition one is dealing with, as will also the physical examination.

Dr. Guest comments that the loss of potassium and nitrogen cannot altogether be accounted for on the basis of what happens in tissues; I assume he means muscular tissue. I agree. Undoubtedly some of the potassium loss reflects the loss incident to the utilization of all the body glycogen. However, in terms of therapy, that also is potassium which it may be essential to replace as one administers dextrose.

Dr. McCune has asked me to read slowly what I said concerning the composition of the solution that we use. First, let me stress that we start by giving half-isotonic solution of sodium chloride or a mixture of two parts of half-isotonic solution of sodium chloride and 1 part of one-twelfth-molar sodium lactate in 5 per cent dextrose solution, in a dosage of 10 to 15 cc. per kilogram of body weight. These solutions are adequate to repair acidosis, if acidosis is present. If one is sure the baby has alkalosis, as probably is true in pyloric stenosis, then one should use half-isotonic solution of sodium chloride alone without diluting it with sodium lactate solution. That is given in order to accelerate the patient's circulation and to start a flow of urine, so that there will be no trouble when the potassium-containing solution is administered. The potassium-containing solution that I use —there is nothing magic about it, of course—happens to be sodium lactate 2.2 Gm., sodium chloride 0.58 Gm., potassium chloride 0.9 Gm. and dipotassium phosphate 0.25 Gm. added to a liter of 10 per cent dextrose solution. It is important to stress "added to." It is not advisable to keep a potassium-containing solution sitting in a ward or in a parenteral fluid supply room. Somebody will pick up the solution, not realizing it contains potassium, and there will be an accident. So these salts are made up, as I have given them, in a little flask, which is autoclaved. It is such a little flask that no other flask that has anything to do with parenteral fluid resembles it. At the time the house officer sets up his drip apparatus, he takes the flask of salts and himself pours it into a liter of 10 per cent dextrose solution. In that manner safety from accidents is assured.

Dr. Katharine Dodd, Cincinnati: I agree with Dr. Butler that in many instances the determination of the carbon dioxide is overstressed and that the degree of dehydration is often more important than the acidosis. Nevertheless, I have found babies who have received no bicarbonate before admission but who were alkalotic instead of acidotic. In Cincinnati many physicians give babies with diarrhea bicarbonate solution, hence some of the babies have been extremely alkalotic on admission. I have also seen babies who were so acidotic that it does not seem possible they could have recovered without correction.

I would add to the list of chemical determinations which one wishes to have on admission that of nonprotein nitrogen. Many of the babies who are extremely dehydrated have poor renal function and pronounced retention of nitrogenous waste products. My associates and I have found that when such babies are given large quantities of fluid they do much better than when they are given the usual amount.

I should like to compliment Dr. Butler on his house staff. Sixty-two days of intravenous therapy has never been approached in our hospital. He must have an efficient house staff if they are able to give a newborn baby with diarrhea intravenous therapy for sixty-two days.

Erythroblastosis Fetalis: Accurate Diagnosis by New Tests. DR. L. K. DIAMOND and DR. N. M. ABELSON, Boston.

New and accurate laboratory tests are now available to supplement clinical and pathologic criteria in differentiating erythroblastosis fetalis from conditions with which it was formerly confused. Clinical findings in erythroblastosis fetalis are variable. They include splenomegaly and hepatomegaly, which may or may not be detectable; anemia, which in some cases appears early and in other cases late; early jaundice, which may or may not be present, and edema, which is rare. An excessive number of erythroblasts is not invariably found in the peripheral blood. A history of transfusion for the mother or of clinical evidence of erythroblastosis fetalis in siblings with increasing severity of the disease in succeeding children aids in evaluating the clinical observations.

Pathologic evidence is also variable. The most significant findings are icteric staining of body tissues and fluids, kernicterus, pallor, enlarged spleen and liver, extramedullary hemopoiesis, hemosiderosis and the presence of large numbers of erythroblasts in the blood vessels.

Laboratory tests are designed to show evidence of: (1) incompatibility between maternal and fetal bloods, (2) active maternal sensitization to fetal antigen, (3) passive transfer of maternal antibodies to the infant and (4) combination of such antibodies with fetal antigen. The various methods of blood typing are helpful in demonstrating fetal-maternal incompatibility. Examination of the maternal serum for agglutinins against fetal red cells may yield evidence of active maternal sensitization. Agglutinins not appreciable in saline diluents may be detected in protein mediums. The presence of abnormal agglutinins in the child's serum indicates that passive transfer of maternal antibodies has occurred. A laboratory diagnosis of erythroblastosis fetalis cannot be made from evidence of abnormal agglutinins in the maternal or fetal serum without proof that the mother's and the infant's blood are incompatible. There are now three methods of showing combination of fetal red cells with maternal agglutinins. Resuspension of the infant's cells in appropriate diluents, such as 20 per cent albumin, will often bring about rapid agglutination of these cells. Observation of the behavior of fetal cells at oil and water interfaces may also be useful for detecting sensitization. In certain cases the reagglutination phenomenon, that is, the agglutination of fresh Rh-positive cells by antibodies attached to fetal erythrocytes, may be apparent.

DISCUSSION

DR. A. ASHLEY WEECH, Cincinnati: I should like to ask Dr. Diamond if he has at his disposal any signs or symptoms that may be noted during the early days of the infant's life which will tell him in advance which of these babies are going to be mentally defective and which are not. I have on my conscience several babies, since, in directing the plan of therapy, I feel that I am personally responsible for having saved the lives of infants who subsequently turned out to be mentally defective.

DR. CARL H. SMITH, New York: Dr. Diamond has made an excellent presentation and a contribution which will facilitate an earlier and more accurate diagnosis of erythroblastosis fetalis.

With the renewed interest in this condition there are now many aspects of this disease that await clarification. Extremely important is the proper management of the baby whose blood is Rh positive and whose mother is Rh negative and who manifests the clinical features of erythroblastosis except that the hemoglobin content and the red blood count are normal. It is not always possible to determine within a short time the titer of maternal agglutinins or "blocking" antibodies, although available information indicates that the prognosis appears to be related to their concentration. Yet it is the deeply jaundiced infant with normal blood levels at birth whose chances for survival may be poor. Treatment by exsanguination and transfusion requires great technical skill. On the other hand, this drastic treatment may be unnecessary, as was illustrated by an infant observed recently with fetal erythroblastosis and high normal levels of hemoglobin and red cells who was jaundiced at birth but who recovered without treatment during the stay in the hospital.

It seems probable that with the new procedures devised by Dr. Diamond, such as the oil suspension test, it will be possible to separate those infants in this group who require no treatment from those for whom treatment is urgent. In this connection I should like to ask Dr. Diamond if he can explain the phenomenon of the simultaneous presence of "blocking" or inhibitor antibodies and of albumin in the circulation without destruction of the red blood cells even at short intervals.

I should like to know what Dr. Diamond regards as desirable blood levels to be maintained by transfusions. It has been my practice to administer sufficient blood to the newborn infant to support levels of 10 to 12 Gm. of hemoglobin per hundred cubic centimeters of blood, which is the range for normal infants, rather than values of 16 to 20 Gm., such as characterize the early newborn period.

In an infant with erythroblastosis whom I studied recently in whom the Rh and Hr factors were not related to eythroblastosis, the mother's blood belonged to group O and the infant's to group A. The titer for anti-A in the mother's serum was 1:624. Before regarding this titer as of etiologic significance, it seemed important to compare it with the concentrations which experience has shown contribute to the pathogenesis of this disease. Are data available which indicate the normal and abnormal levels of anti-A and anti-B agglutinins resulting from isoimmunization of the mother? As a final point it may be stated that with the introduction of the more appropriate terminology of hemolytic anemia of the newborn for fetal erythroblastosis, the designation of "congenital anemia of the newborn" as a separate type is no longer required; the latter may be regarded as one of the less severe forms of this disease.

DR. LOUIS K. DIAMOND, Boston: Obviously there are many questions we cannot as yet answer. Some of the tests I have mentioned will help direct further lines of investigation and will answer these questions in the future.

In reply to Dr. Carl Smith's question as to why some of the most severely affected patients die suddenly on the fifth day when there was no evidence of hemolysis on the first day: No precise reason for this is now known. Among the possibilities, however, are: 1. That the plasma proteins of the fetus are different from those of the infant after birth and that as they change to the more mature form the interaction between the antibody passively transferred from the mother and the baby's Rh-positive cells begins to take place. Certainly this is demonstrable in the test tube by the addition of albumin or serum to sensitized cells or to the mixture of Rh-positive cells and hyperimmune or heat-stable (blocking) antibodies. 2. The mother may pass on to the child some protective substances which are deteriorated or which disappear during the first five days.

As to the use of transfusion for these patients, we are guided entirely by the patient's course; that is, we do not use transfusion at present except when anemia begins to develop unless the heroic measure of exsanguinating the patient at birth or shortly thereafter and replacing the blood with fresh blood is taken. Ordinarily after the third or fourth day we are satisfied with a level of about 12 Gm. of hemoglobin per hundred cubic centimeters, and after the first week, with even

as little as 9 or 10 Gm. of hemoglobin if the patient seems to be doing well. We are guided in the use of transfusion by the patient's course.

As to the variety of terms that have been used for the disease, every person who reports a case is partial to his own nomenclature or develops a new one. Until an adequate and logical nomenclature is settled on, the term erythroblastosis fetalis, with the varieties of severe anemia, icterus gravis familiaris and fetal hydrops, should be used.

We have noted more than 20 cases in which the mother had an anti-A or anti-B agglutinin titer of over 1,000, and the baby had not the slightest evidence of hemolytic anemia. The mere presence of a high titer of anti-A or B agglutinins in the mother's blood against the baby's red cells is no proof that disease is going to develop or that erythroblastosis is or was present.

In answer to Dr. Weech's question as to which infants can be judged mentally damaged early, we expect regularly and have found in every case so far that an infant in whom opisthotonos or spasticity or even convulsions develop within the first week or ten days will be defective. We have never seen an infant of that sort survive and be adequate in any respect. There are milder degrees of damage of the brain that do not show themselves early by opisthotonos or spasticity but usually appear as the infant begins to develop after the first six months.

Vitamin A Studies of Pregnant Women and of Newly Born Infants.
Dr. J. M. Lewis and Dr. Oscar Bodansky.

In a previous communication, we have reported that during the last trimester of pregnancy there is a fall in the concentration of vitamin A in the blood plasma. The most likely explanation for this phenomenon is the high demands for vitamin A made by the fetus on the mother. Thus, considerable quantities of vitamin A were found to be stored in the livers of the newborn infants.

The present study was undertaken to determine whether moderate supplements of vitamin A and of carotene (10,000 U. S. P. units of vitamin A daily) during the last few months of pregnancy would prevent the fall in vitamin A concentration in the blood. An opportunity was also afforded to study the effect of these supplements on the concentration of vitamin A in the blood of the newborn infant.

The results of this study revealed that the daily use of vitamin A or of carotene supplements prevented the fall in the concentration of vitamin A during the last trimester of pregnancy. On the other hand, the vitamin A and carotene values of cord blood were no higher in women receiving daily supplements of vitamin A or of carotene than in those receiving no supplements. Furthermore, huge amounts of vitamin A (500,000 units) administered during labor brought about considerable rises in its concentration in the maternal blood but had no appreciable effect on its concentration in the blood of the newborn infant. Examination of the placenta revealed no deposit of vitamin A in this organ following the administration of this enormous amount.

At first glance it would seem that the lack of rise of vitamin A in the cord blood in the presence of considerable elevations in the maternal blood may be attributed to the limited ability of the placenta to transmit vitamin A to the fetus. On the other hand, the possibility exists that the vitamin A–regulatory mechanism of the fetus is such that in spite of considerable amounts of the substance going through the placenta, its concentration may not be elevated in the cord blood. A preliminary experiment which we carried out in guinea pigs seems to support the latter possibility. Thus, when exceedingly large quantities of vitamin A were given to pregnant guinea pigs the blood levels in the newborn animals were not elevated. However, considerable storage of vitamin A was found in the livers of the newborn guinea pigs, indicating good transmission of vitamin A through the placenta. It would seem that in the guinea pig the liver withdraws vitamin A so efficiently and rapidly that transmission of the substance through the placenta is not reflected in increased concentration in the blood of the newborn. Further experiments are being conducted along these lines.

DISCUSSION

DR. A. ASHLEY WEECH, Cincinnati: I should like to ask Dr. Lewis if he has any information on changes in blood lipids during pregnancy and on blood lipid values in the serum of the newborn infant. I have looked on the fat-soluble substances not as existing in the aqueous phase of the circulation but as being in solution in the blood lipids, and I wonder whether if these values were expressed in milligrams or units per gram of blood lipids some of the discrepancies in concentration might not disappear.

This has nothing to do, of course, with the beautiful demonstration of the effect of feeding the mother on the storage of vitamin A in the infant.

DR. JOSEPH STOKES, JR., Philadelphia: I simply wish to add to the observations on vitamin A in acute hepatitis. My associates and I have selected volunteers and have followed their blood level of vitamin A over a period of months. We have found with the first symptoms of onset of acute hepatitis an immediate drop in vitamin A, which in most instances precedes any other evidence to be obtained by tests. This, of course, is not an index of the function of the liver, but it is added evidence of a decided effect on the liver. This work was confirmed later by Hoagland. I think there is an extraordinary drop under these conditions.

DR. J. M. LEWIS, New York: Dr. Weech, we carried out no studies on the concentration of the blood lipids during pregnancy or during the newborn period. It would be worth while to find out whether there is any parallelism in the behavior of vitamin A and of lipids during the course of pregnancy. In this connection, it is of interest to note that, whereas the concentration of vitamin A in the blood falls during the last trimester of pregnancy, the carotene levels are sustained during this period.

Correspondence

SCARLET FEVER AMONG PUEBLO INDIANS

To the Editor:—Failure to observe the occurrence of a disease assumed to be common should not be assumed to indicate its complete absence or the complete immunity to it of a people, unless they be entirely isolated. The comparative lack of cases (observed by physicians or nurses) of scarlet fever among Indians of the Southwest has been the basis for suggestions of natural immunity, both written and oral, for many years.

Frank and Elkin, having found 22 per cent positive reactions to the Dick test among 816 Indian children (750 Pueblo and 66 Navajo), concluded that they should be susceptible to the disease, and observed 8 cases in the region of Laguna, N. Mex., during 1945 (Am. J. Dis. Child. **71**:477 [May] 1946). Wider and more detailed observation, in their opinion, probably would increase the recorded incidence of the disease in these people. The following observations among another branch of the Pueblos tend to support their thesis:

The Zuni branch of the Pueblos is a group of approximately 2,500 persons, dwelling in extremely close quarters in one main and three outlying village groups. The main village is some 40 miles (64.4 kilometers) from Gallup, N. Mex., and contacts with Gallup and with Albuquerque are frequent and numerous. During the months of February, March and April, 1946, 24 cases of clinical scarlet fever were observed in Zuni. These were limited to fifteen family groups, none having more than 3 cases, most not more than 2. Sixteen cases occurred in February, the remainder being scattered, but most of them in a secondary peak during March.

Age incidence varied from 2 years to 22 years, with two thirds of all cases in children under 10 years. Symptoms were typical of scarlet fever: acute onset, with fever, headache and sore throat, glossitis, and a fine erythematous rash prominent on the body. Desquamation usually followed after seven to ten days. In most cases the disease was mild, with little toxicity and of short duration. Complications were limited to 2 cases with transient edema and 1 with cervical adenitis which did not suppurate.

All patients were seen, and most of them treated with small doses of sulfadiazine (a total dosage of approximately 6 to 12 Gm.) by the field nurse. Most patients were seen also by the physician, who had spent several years among the Navajo Indians without having encountered (clinical) scarlet fever and was much interested to observe the destruction of the myth that it does not occur among fullblood Indians.

At a staff meeting of the physicians of the Navajo Service, held about a year before, this point was discussed at some length. Only one of the physicians then present had observed cases of scarlet fever among the Navajos (Sedlacek, B., and Molholm, C.: Personal communications to the author). He cited 3 cases personally observed, all having stemmed from contact with the daughter of a trader on the reservation. Suggestions as to the reasons for the absence of the rash from cases that otherwise would have fitted the picture of the disease included (1) absence of the erythrotoxic factor from the particular strains of streptococci involved (but by definition, scarlet fever must present a rash), and (2) absence of the (allergic?) factor responsible for the patient's dermal reaction to the streptococcus.

Scarlet fever does occur among fullblood Indians, at least among the Pueblos; whether the Navajos also present the same clinical destruction of a medical myth must await further observations.

J. K. NEWTON, M.D.

Medical Officer, Zuni Indian Hospital, Zuni, N. Mex.

To the Editor:—Dr. Newton's report is interesting and offers further evidence of the existence of scarlet fever among the Pueblos.

In January 1945, I performed Dick tests on 215 Navajo children at the Toadalena boarding school in Toadalena, N. Mex. Twelve per cent were positive reactors, indicating that susceptibilty is present among the Navajo children as well as the Pueblos.

In considering scarlet fever among the Navajos one must remember their greater isolation, living in scattered hogans rather than villages, and the mode of transmission of scarlet fever. With these two factors in mind, the incidence of the disease should be less amongst them than among the Pueblos or the white population.

M. L. FRANK, M.D.

Indian General Hospital, Albuquerque, N. Mex.

Directory of Pediatric Societies *

INTERNATIONAL

International Association of Preventive Pediatrics

President: Prof. S. Monrad, Dronning Louises Børnehospital, Copenhagen, Denmark.
Secretary: Dr. Daniel Oltramare, 15 Rue Lévrier, Geneva, Switzerland.

International Congress of Pediatrics

President: Dr. Henry F. Helmholz, Mayo Clinic, Rochester, Minn.
Secretary-General: Dr. L. Emmett Holt Jr., 477 First Ave., New York 16.
Canadian Committee:
Chairman: Dr. Alan Brown, Hospital for Sick Children, 67 College St., Toronto 2.
Secretary: Dr. S. G. Ross, 1390 Sherbrooke St. W., Montreal.
Place: New York. Time: Sept. 16-19, 1947.

International Congress for the Protection of Infancy

Secretary: Prof. G. B. Allaria, Corso Bramante 29, Torino 120, Italy.

Save the Children International Union

President: Mrs. Gordon Morier.
Secretary: Dr. Georges Thélin, 43 Quai Wilson, Geneva, Switzerland.
Place: Geneva, Switzerland. Time. Sept. 17-20, 1946.

FOREIGN

Argentine Pediatric Society of Buenos Aires

President: Dr. Martin Ramón Arana, 1809 Rodriguez Peña, Buenos Aires.
General Secretary: Dr. Alfredo Larguia, Cerrito 1179, Buenos Aires.

Associação Paulista de Medicina, Secção de Pediatrias

President: Dr. Vicente Lara.
First Secretary: Dr. Armando de Arruda Sampaio.
Second Secretary: Dr. Luiz Augusto Monteiro Toledo, Av. Brigadeiro Luiz Antonio 393, 1° Andar, São Paulo, Brazil.
Time: Twelfth of every month, 8:30 p. m.

British Paediatric Association

President: Prof. G. B. Fleming, 13 Lynedoch Crescent, Glasgow.
Joint Secretary: Prof. Alan Moncrieff and Dr. Donald Paterson, Hospital for Sick Children, Great Ormond St., London, W. 1.
Place: Rugby School, Rugby. Time: Aug. 1-3, 1946.

Danish Pediatric Society

President: Dr. E. Lenstrup, Copenhagen.
Secretary: Dr. Gjørup, Dronning Louises Børnehospital, Copenhagen.

Nederlandische Vereeniging voor Kindergeneeskunde

President: Dr. J. H. G. Carstens, Servaas Bolwerk 14, Utrecht.
Secretary: Dr. R. P. van de Kasteele, Lyceumplein 10, den Haag.
Place: Children's Hospital or Pediatric Clinic. Time: Three times a year.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

PALESTINE JEWISH MEDICAL ASSOCIATION, SECTION OF PHYSICIANS OF CHILDREN'S DISEASES

President: Prof. L. F. Meyer, 29 Toelsohn St., Tel Aviv.
Secretary: Dr. A. Brünn, 9 Maazestre, Tel Aviv.

ROYAL SOCIETY OF MEDICINE, SECTION FOR THE STUDY OF DISEASE IN CHILDREN

President: Prof. Norman Capon, 49A Rodney St., Liverpool, England.
Secretary: Dr. J. N. O'Reilly, 46 Harley St., London, W. 1, England.
Place: 1 Wimpole St., London. Time: Fourth Friday of each month, 4:15 p. m.

SOCIEDAD CUBANA DE PEDIATRIA

President: Dr. Teodosio Valledor, Habana.
Secretary: Dr. Carlos Hernandez Miyares, Hospital Nuestra Señora de las Mercedes L y 21, Apartado, 2430, Habana.
Place: Cátedra de Clinica Infantil, Hospital Nuestra Señora de las Mercedas y Hospital Municipal de Infancia, Habana. Time: Last Wednesday of every month.

SOCIEDAD ECUADORIANA DE PEDIATRIA

President: Dr. Francisco de Icaza Bustamente.
Secretary: Dr. M. I. Gómez Lince, P. O. Box 693, Guayaquil.

SOCIEDAD MEXICANA DE PEDIATRIA

President: Dr. Luis Berlanga Berumen, Bucareli No. 85, Altos, Mexico.
Secretary: Dr. Jésus Alvarez de los Cobos, Ignacio Mariscal 124, Mexico.

SOCIEDAD DE PEDIATRIA DE CÓRDOBA

President: Dr. Juan Francisco Herrera, Córdoba, Argentina.
Secretary: Dr. Bernardo Serebrinsky, Dean Funes 2000, Esq. Ocaña (N.), Córdoba. Argentina.
Place: Comite pro Defenso del Niño, Dean Funes 2000, Córdoba, Argentina. Time: Once a month.

SOCIEDAD DE PEDIATRIA DEL LITORAL

President: Dr. Jose E. Celoria, Hospital Centenario, Rosario, Argentina.
Secretary: Dr. Gloria Lovell, Hospital Centenario, Rosario, Argentina.

SOCIEDAD DE PEDIATRÍA DE SANTIAGO DE CUBA

President: Dr. Antonio Béguez César, Sagarra 107, Santiago de Cuba.
Secretary: Dra. Susana Texdó Vaillant, Padre Pico 57, Santiago de Cuba.
Place: Colegio Médico. Time: Last Tuesday of every month.

SOCIEDAD VENEZOLANA DE PUERICULTURA Y PEDIATRIA

President: Dr. Pedro J. Alvarez.
Secretary: Dr. Ernesto R. Figueroa, 3a Avenida 10, Bella Vista, Caracas.
Place: Hospital Municipal de Niños Jose Manuel de los Rios, Caracas.

SOCIÉTÉ DE PÉDIATRIE DE PARIS

President: Dr. Leveuf, Paris, France.
Secretary: Dr. Jean Hallé, 10 bis Rue Pré aux Clercs, Paris, France.
Place: Hôpital des Enfants Maladies, 149 Rue de Sèvres. Time: 4:30 p. m., third Thursday of every month.

SWEDISH MEDICAL SOCIETY, SECTION FOR PEDIATRICS AND SCHOOL HYGIENE

President: Prof. Arvid Wallgren, 53 Strandvägen, Stockholm.
Secretary: Dr. Henning Magnusson, 58 Odengatan, Stockholm.
Place: Various clinics and hospitals in Stockholm and Uppsala. Time: Second Friday of each month (except summer).

Uruguayan Society of Pediatrics

President: Dr. Jose Bonaba, Montevideo.
Secretary: Dr. Héctor Fossatti, Durazno 1882, Montevideo.
Place: Club Medico del Uruguay, Avenida Agraciado 1464 (Piso 13), Montevideo

NATIONAL

American Medical Association, Scientific Assembly, Section on Pediatrics

Chairman: Dr. John Aikman, 184 Alexander St., Rochester, N. Y.
Secretary: Dr. Gilbert J. Levy, 188 S. Bellevue Blvd., Memphis, Tenn.

American Academy of Pediatrics

President: Dr. Jay I. Durand, 515 Cobb Bldg., Seattle, Wash.
Secretary: Dr. Clifford G. Grulee, 636 Church St., Evanston, Ill.
Place: Hotel William Penn, Pittsburgh. Time: Nov. 13-16, 1946.

American Hospital Association, Massachusetts Hospital Association

Chairman: Dr. Frank Wing, Boston.
Secretary: Dr. W. Franklin Wood, McLean Hospital, Waverly 79, Mass.
Place: Boston. Time: November 1946.

American Pediatric Society

President: Dr. Harold K. Faber, 2361 Clay St., San Francisco.
Secretary-Treasurer: Dr. Henry G. Poncher, 1819 W. Polk St., Chicago 12.

Canadian Society for the Study of Diseases of Children

President: Dr. H. S. Little, 300 Dufferin Ave., London, Ontario.
Secretary-Treasurer: Dr. Elizabeth Chant Robertson, 67 College St., Toronto 2.
Place: Banff, Alberta. Time: June 14-15, 1946.

Society for Pediatric Research

President: Dr. Mitchell I. Rubin, 219 Bryant St., Buffalo 9, N. Y.
Secretary: Dr. Robert F. Ward, Bellevue Hospital, New York 16.

SECTIONAL

Intermountain Pediatric Society

President: Dr. Robert Alway, University of Utah School of Medicine, Salt Lake City 2.
Secretary-Treasurer: Dr. L. Paul Rasmussen, 1020 Boston Bldg., Salt Lake City 1.
Place: Salt Lake City General Hospital. Time: First Thursday of each month, 8 p. m.

New England Pediatric Society

President: Dr. James Marvin Baty, 1101 Beacon St., Brookline, Mass.
Secretary-Treasurer: Dr. Charles D. May, 300 Longwood Ave., Boston.
Place: Boston Medical Library. Time: Three meetings a year, occurring from September to May.

North Pacific Pediatric Society

President: Dr. Percy Guy, 502–2d Ave., Seattle, Wash.
Secretary: Dr. Aldis B. Johnson, 515 Cobb Bldg., Seattle, Wash.
Place: Vancouver, B. C. Time: Oct. 19, 1946.

Northwestern Pediatric Society

President: Dr. George Kimmel, Redwing, Minn.
Secretary-Treasurer: Dr. Northrop Beach, 1009 Nicollet Ave., Minneapolis.
Place: Minneapolis, St. Paul, Duluth and Rochester. Time: January, April, July and October.

Rocky Mountain Pediatric Society

President: Dr. G. R. Fisher, 23 E. Pikes Peak Ave., Colorado Springs, Colo.
Secretary: Dr. Joseph H. Lyday, 1850 Gilpin St., Denver 2.

Southern Medical Association, Section of Pediatrics

Chairman: Dr. Stewart H. Welch, 117 S. 20th St., Birmingham 5, Ala.
Secretary: Dr. W. Ambrose McGee, 1601 Monument Ave., Richmond 20, Va.
Place: Miami, Fla. Time: Nov. 4-7, 1946.

STATE

Alabama Pediatric Society

President: Dr. Jerome C. Chapman, 2160 Highland Ave., Birmingham.
Secretary-Treasurer: Dr. Ruth Berrey, 2021–6th Ave. N., Birmingham.
Place: Birmingham. Time: September 1946.

Arizona Pediatric Society

President: Dr. W. P. Sherrill, 342 W. McDowell Rd., Phoenix.
Secretary: Dr. W. F. Schoffman, 926 E. McDowell Rd., Phoenix.
Place: Phoenix or Tucson. Time: At time of state meeting.

Arkansas State Pediatric Association

Chairman: Dr. C. B. Billingsley, 1425 N. 11th St., Fort Smith.
Secretary: Dr. R. E. Weddington, 1425 N. 11th St., Fort Smith.

California State Medical Society, Section on Pediatrics

Chairman: Dr. Charles W. Leach, 2000 Van Ness Ave., San Francisco 9.
Secretary: Dr. Chester I. Mead, 1930 Truxton Ave., Bakersfield.
Place: Biltmore Hotel, Los Angeles. Time: May 7-10, 1946.

Florida State Pediatric Society

President: Dr. Councill Rudolph, 103–5th St. S., St. Petersburg.
Secretary: Dr. Robert Blessing, 409 Blount Bldg., Ft. Lauderdale.
Place: Concurrent with state association convention and fall meeting.

Georgia Pediatric Society

President: Dr. Alton Johnson, 102 E. Central Ave., Valdosta.
Secretary-Treasurer: Dr. Don F. Cathcart, 478 Peachtree St. N. E., Atlanta.
Place: Atlanta. Time: At time of annual state meeting.

Hezekiah Beardsley Pediatric Club of Connecticut

President: Dr. Edward T. Wakeman, 129 Whitney Ave., New Haven.
Secretary: Dr. Herman Yannet, Southbury Training School, Southbury.
Place: New Haven. Time: September 1946.

Illinois State Medical Society, Section on Pediatrics

Chairman: Dr. Craig D. Butler, 715 Lake St., Oak Park.
Secretary: Dr. A. J. Fletcher, 139 N. Vermilion, Danville.

Indiana State Pediatric Society

President: Dr. K. T. Knode, 1105 E. Jefferson Bldg., South Bend.
Secretary-Treasurer: Dr. Matthew Winters, 621 Hume Mansur Bldg., Indianapolis.
Time: Two meetings a year.

Iowa Pediatric Society

President: Dr. Arnold M. Smythe, 406–6th Ave., Des Moines.
Secretary-Treasurer: Dr. James Dunn, 414 Blackhawk Hotel, Davenport.
Place: Des Moines. Time: April 18, 1946.

LOUISIANA STATE PEDIATRIC SOCIETY

President: Dr. S. George Wolfe, 1560 Line Ave., Shreveport.
Secretary-Treasurer: Dr. W. C. Rivenbark, 1448 Louisiana Ave., New Orleans 15.

MEDICAL SOCIETY OF STATE OF NEW YORK, SECTION ON PEDIATRICS

Chairman: Dr. Carl H. Laws, 12 Pierrepont St., Brooklyn, N. Y.
Secretary: Dr. George R. Murphy, 292 Madison Ave., New York.
Place: Hotel Pennsylvania, New York. Time: May 2-3, 1946.

MEDICAL SOCIETY OF THE STATE OF PENNSYLVANIA, PEDIATRIC SECTION

Chairman: Dr. Elwood W. Stitzel, 403 Central Trust Bldg., Altoona, Pa.
Secretary: Dr. P. F. Lucchesi, Philadelphia Hospital, Philadelphia.

MICHIGAN STATE MEDICAL SOCIETY, PEDIATRIC SECTION

Chairman: Dr. Donald J. Barnes, 3001 W. Grand Blvd., Detroit, Mich.
Secretary: Dr. Mark F. Osterlin, Central Michigan Children's Clinic, Traverse City.
Place: Detroit. Time: Sept. 25-27, 1945.

MISSISSIPPI STATE PEDIATRIC SOCIETY

President: Dr. Harvey F. Garrison Jr., 315 E. Capitol Pl., Jackson.
Secretary: Dr. Guy Verner, 126 N. Congress St., Jackson.

NEBRASKA PEDIATRIC SOCIETY

President: Dr. John M. Thomas, 1418 Medical Arts Bldg., Omaha 2.
Secretary-Treasurer: Dr. Gerald C. O'Neil, 640 City National Bank Bldg., Omaha.
Place: As announced by committee. Time: Third Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

NEW MEXICO STATE PEDIATRIC SOCIETY

President: Dr. M. K. Wylder, 221 W. Central Ave., Albuquerque.
Secretary-Treasurer: Dr. Ly Werner, 221 W. Central Ave., Albuquerque.

NORTH CAROLINA PEDIATRIC SOCIETY

President: Dr. Charles R. Bugg, Professional Bldg., Raleigh.
Secretary: Dr. Charles F. Williams, 817 Hillsboro St., Raleigh.
Place: Roaring Gap. Time: September 1946.

NORTHERN CALIFORNIA PEDIATRIC SOCIETY

President: Dr. Edith M. Meyers, 431–30th St., Oakland.
Secretary: Dr. A. L. Gleason, 411–29th St., Oakland 9.
Place: San Francisco. Time: Second Thursday of February, April, September and November.

OKLAHOMA STATE PEDIATRIC SOCIETY

President: Dr. G. R. Russell, 604 S. Cincinnati Ave., Tulsa.
Secretary: Dr. Luverne Hays, 108 W. 6th St., Tulsa.
Place: With Oklahoma State Medical Association. Time: Annual Meeting.

SOUTH CAROLINA PEDIATRIC SOCIETY

President: Dr. George D. Johnson, Spartanburg.
Secretary-Treasurer: Dr. B. O. Ravenel, Roper Hospital, Charleston.

TENNESSEE PEDIATRIC SOCIETY

President: Dr. F. T. Mitchell, 376 S. Bellview, Memphis.
Secretary-Treasurer: Dr. W. O. Vaughan, 2103 Hayes St., Nashville 5.
Time: Second Monday in April.

Texas Pediatric Society

President: Dr. Max Woodward, 202 N. Travis St., Sherman.
Secretary-Treasurer: Dr. John E. Ashby, 3610 Fairmount Ave., Dallas 4.
Place: Fort Worth. Time: Oct. 4-5, 1946.

Virginia Pediatric Society

President: Dr. Emily Gardner, 1100 W. Franklin St., Richmond 20.
Secretary: Dr. Louise Galvin, 214 S. Boulevard, Richmond 21.

West Virginia State Medical Society, Section on Pediatrics

President: Dr. Jack Basman, 1021 Quarrier St., Charleston.
Secretary: Dr. Harry E. Baldock, Medical Arts Bldg., Charleston.
Place: Huntington. Time: May 13-15, 1946.

LOCAL

Academy of Medicine of Cleveland, Pediatric Section

Chairman: Dr. J. I. Hartman, 10515 Carnegie Ave., Cleveland.
Secretary: Dr. Alexander N. Freed, 2012 W. 25th St., Cleveland.
Place: Cleveland Medical Library Bldg. Time: 8:15 p. m., October, December, February and April.

Academy of Medicine, Toronto, Section of Pediatrics

President: Dr. J. H. Ebbs, 13 Queen's Park, Toronto, Canada.
Secretary: Dr. J. F. McCreary, 170 St. George St., Toronto, Canada.
Place: Academy of Medicine. Time: 8:30 p. m., third Thursday of each month.

Bronx Pediatric Society

President: Dr. Walter Levy, 12 E. 88th St., New York.
Secretary: Dr. Joseph Blasenstein, 960 Grand Concourse, New York.
Place: Concourse Plaza Hotel, 161st St. and Grand Concourse. Time: Second Wednesday of each month, except June, July, August and September.

Brooklyn Academy of Pediatrics

President: Dr. Lambert Krahulik, 14 Sidney Pl., Brooklyn.
Secretary: Dr. Joseph Battaglia, 713 Bushwick Ave., Brooklyn 21.
Place: Granada Hotel. Time: 8:45 p. m., fourth Wednesday of February, March, April, May and November.

Buffalo Pediatric Society

President: Dr. Douglas P. Arnold, 159 Bidwell Parkway, Buffalo, N. Y.
Secretary: Dr. Richard A. Downey, 786 Forest Ave., Buffalo 9, N. Y.
Place: Children's Hospital, 219 Bryant St. Time: 8:30 p. m., first Monday of each month from September to June.

Central New York Pediatric Club

President: Dr. Arthur W. Benson, 2 St. Paul St., Troy.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Places: Various cities in New York. Time: Third Tuesday of April and October.

Chicago Pediatric Society

President: Dr. Joseph Greengard, 4753 Broadway, Chicago 40.
Secretary: Dr. Alvah L. Newcomb, 723 Elm St., Winnetka, Ill.
Place: Children's Memorial Hospital, 710 Fullerton Ave. Time: Third Tuesday of each month, October to May inclusive.

Cincinnati Pediatric Society

President: Dr. Leo S. Friedman, 666 Rockdale Ave., Cincinnati 29.
Secretary: Dr. George Renner, 3144 Jefferson Ave., Cincinnati.
Place: Children's Hospital, Elland Ave., Cincinnati. Time: On call.

Dallas Pediatric Society

President: Dr. O. René Caillet, 4325 Cole Ave., Dallas, Texas.
Secretary-Treasurer: Dorothy Wyvell, Bradford Memorial Hospital for Babies, Texas.
Place: Children's Medical Center. Time: 1 p. m., third Saturday and 8:30 p. m., the first Thursday of each month.

Detroit Pediatric Society

President: Dr. Otto Grob, 651 Fisher Bldg., Detroit 2, Mich.
Secretary: Dr. Harold B. Rothbart, 773 Fisher Bldg., Detroit 2, Mich.
Place: Variable. Time: Third Wednesday of each month.

Houston Pediatric Society

President: Dr. Raymond Cohen, 2300 Caroline St., Houston, Texas.
Secretary: Dr. Betty Moody, 526 Richmond Rd., Houston, Texas.
Place: River Oaks Country Club. Time: 7:30 p. m., fourth Monday of each month.

Kansas City (Missouri) Pediatric Society

President: Dr. Harry M. Gilkey, 1624 Professional Bldg., Kansas City.
Secretary: Dr. Leland Speer, 1022 Parkway, Kansas City.
Place: Kansas City General Hospital. Time: On call.

Los Angeles County Medical Association, Pediatric Section

President: Dr. Albert L. Hill, 1401 S. Hope St., Los Angeles.
Secretary-Treasurer: Dr. Robert Simonds, 1925 Wilshire Blvd., Los Angeles.
Place: Los Angeles County Medical Headquarters, 1925 Wilshire Blvd. Time: Second Monday of February, April, June, October and December.

Medical Society of the County of Kings and the Academy of Medicine of Brooklyn, Pediatric Section

President: Dr. Henry Ràscoff, 895 Eastern Parkway, Brooklyn.
Secretary: Dr. Harold Levy, 750 St. Marks Ave., Brooklyn.
Place: 1313 Bedford Ave., Brooklyn. Time: 9:00 p. m., fourth Monday of each month.

Medical Society of the County of Queens, Inc., Section on Pediatrics

Chairman: Dr. Meyeron Coe, 217-02–91st Ave., Queens Village, N. Y.
Secretary-Treasurer: Dr. Loùis Appel, 143-42 Cherry Ave., Flushing, N. Y.
Place: Queens County Medical Bldg., Forest Hills, N. Y. Time: Third Monday of October, January, March and May.

Medical Society of the District of Columbia, Section on Pediatrics

President: Dr. John Washington, 2203 Wyoming Ave., Washington, D. C.
Secretary-Treasurer: Dr. George Maksim, 1418 Good Hope Rd. S.E., Washington, D. C.
Place: Medical Society Bldg., 1718 M St. N. W. Time: 8 p. m., third Thursday of October, January, March and May.

Memphis Pediatric Society

President: Dr. Kinsey M. Buck, 1193 Madison Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. Barton Etter, 1024 Madison Ave., Memphis, Tenn.
Place: Memphis Country Club. Time: 8 p. m., Dec. 13, 1946.

Milwaukee Pediatric Society

President: Dr. G. H. Fellman, 231 W. Wisconsin Ave., Milwaukee.
Secretary-Treasurer: Dr. R. P. Showalter, 411 E. Mason St., Milwaukee 2.
Place: Milwaukee Children's Hospital. Time: Second Wednesday in February, April, June, October and December.

New York Academy of Medicine, Section of Pediatrics

Chairman: Dr. Robert O. Du Bois, 122 E. 76th St., New York.
Secretary: Dr. Harold W. Dargeon, 1095 Park Ave., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from November to May, inclusive, 8:30 p. m.

Oklahoma City Pediatric Society

President: Dr. William M. Taylor, 625½ N. W. 10th St., Oklahoma City.
Secretary: Dr. Jeanne McKinnon-Shofstall, 1019 N. Lee St., Oklahoma City.
Place: Oklahoma Club. Time: Third Thursday of each month.

Philadelphia Pediatric Society

President: Dr. Waldo E. Nelson, Temple University School of Medicine, Philadelphia.
Secretary: Dr. Sherman Little, 1740 Bainbridge St., Philadelphia 46.
Place: College of Physicians, 19 S. 22d St. Time: 8:30 p. m., second Tuesday in October, December, February and April.

Pittsburgh Pediatric Society

President: Dr. Elwood Stitzel, 403 Central Trust Bldg., Altoona, Pa.
Secretary-Treasurer: Dr. C. J. Stoecklein, Medical Arts Bldg., Pittsburgh 13.
Place: Pittsburgh Academy of Medicine. Time: Second Friday in October, December, February and April.

Richmond Pediatric Society

President: Dr. Edwin L. Kendig Jr., 828 W. Franklin St., Richmond 20, Va.
Secretary-Treasurer: Dr. Thomas S. Chalkley, 1200 E. Broad St., Richmond, Va.
Place: Medical College Hospital. Time: 8 p. m., third Thursday of each month, except June, July and August.

Rochester Pediatric Society

President: Dr. William L. Bradford, 260 Crittenden Blvd., Rochester 7, N. Y.
Secretary-Treasurer: Dr. Donald D. Posson, 222 Chili Ave., Rochester 11, N. Y.
Place: Rochester Academy of Medicine or arrangement by program committee.
Time: Third Friday of each month from October to May.

St. Louis Pediatric Society

President: Dr. Joseph C. Jaudon, 337 N. Euclid Ave., St. Louis.
Secretary-Treasurer: Dr. Gilbert B. Forbes, 500 S. Kingshighway, St. Louis 10.
Time: Second Thursday of each month from October to May, inclusive.

Seattle Pediatric Society

President: Dr. Norman W. Murphy, 1300 Madison St., Seattle 4.
Secretary: Dr. David M. Harris, 630 Medical Arts Bldg., Seattle 1.
Place: College Club. Time: Third Friday of each month from September to June at 6:30 p. m.

Southwestern Pediatric Society

President: Dr. Robert J. Dostal, 710 Wilshire Blvd., Santa Monica, Calif.
Secretary: Dr. H. M. Van Dyke, 541 E. Broadway, Long Beach, Calif.
Place: University Club of Los Angeles. Time: 6:30 p. m., first Wednesday in January, March, May, September and November.

University of Michigan Pediatric and Infectious Disease Society

President: Dr. Park Bradshaw, Muskegon, Mich.
Secretary: Dr. Harry A. Towsley, 1313 E. Ann St., Ann Arbor, Mich.
Place: University Hospital, Ann Arbor, Mich. Time: Oct. 25-26, 1946.

Westchester County Medical Society, Pediatrics Section (New York)

President: Dr. John B. Ahouse, 27 Ludlow St., Yonkers, N. Y.
Secretary-Treasurer: Dr. Elvira Ostlund, 64 Highland Rd., Rye, N. Y.
Place: Hospitals of Westchester County. Time: Third Thursday in November, January, March and May.